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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-Q

(Mark One)

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended June 30, 2025
OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Commission File Number: 001-36014

AGIOS PHARMACEUTICALS, INC.
(Exact Name of Registrant as Specified in Its Charter)

Delaware	**26-0662915**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
88 Sidney Street, Cambridge, Massachusetts	**'02139**
(Address of Principal Executive Offices)	**(Zip Code)**

(617) 649-8600
(Registrant's Telephone Number, Including Area Code)

(Former Name, Former Address and Former Fiscal Year, if Changed Since Last Report)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common Stock, Par Value $0.001 per share	**AGIO**	**Nasdaq Global Select Market**

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

Number of shares of the registrant's Common Stock, $0.001 par value, outstanding on July 25, 2025: 58,101,518

AGIOS PHARMACEUTICALS, INC.

FORM 10-Q

FOR THE THREE AND SIX MONTHS ENDED JUNE 30, 2025

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PART I. FINANCIAL INFORMATION

Item 1. Financial Statements (Unaudited)

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Balance Sheets
(Unaudited)

(In thousands, except share and per share data)	June 30, 2025	December 31, 2024
Assets		
Current assets:		
Cash and cash equivalents	$ 80,871	$ 76,247
Marketable securities	858,066	817,463
Accounts receivable, net	4,986	4,109
Inventory	30,848	27,616
Prepaid expenses and other current assets	44,693	40,165
Total current assets	1,019,464	965,600
Marketable securities	400,467	638,321
Operating lease assets	36,785	42,879
Property and equipment, net	10,579	11,675
Other non-current assets	3,942	4,724
Total assets	$ 1,471,237	$ 1,663,199
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 17,532	$ 16,643
Accrued expenses	35,289	46,861
Income taxes payable	—	871
Operating lease liabilities	17,589	16,781
Total current liabilities	70,410	81,156
Operating lease liabilities, net of current portion	31,171	40,207
Other non-current liabilities	101	880
Total liabilities	101,682	122,243
Stockholders' equity:		
Preferred stock, $0.001 par value; 25,000,000 shares authorized; no shares issued or outstanding at June 30, 2025 and December 31, 2024	—	—
Common stock, $0.001 par value; 125,000,000 shares authorized; 74,254,956 shares issued and 58,038,545 shares outstanding at June 30, 2025, and 73,372,696 shares issued and 57,156,285 shares outstanding at December 31, 2024	74	73
Additional paid-in capital	2,521,545	2,493,811
Accumulated other comprehensive income (loss)	655	(1,518)
Treasury stock, at cost (16,216,411 shares at June 30, 2025 and December 31, 2024)	(802,486)	(802,486)
Accumulated deficit	(350,233)	(148,924)
Total stockholders' equity	1,369,555	1,540,956
Total liabilities and stockholders' equity	$ 1,471,237	$ 1,663,199

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Operations
(Unaudited)

(In thousands, except share and per share data)	Three Months Ended June 30, 2025	Three Months Ended June 30, 2024	Six Months Ended June 30, 2025	Six Months Ended June 30, 2024
Revenues:				
Product revenue, net	$ 12,455	$ 8,615	$ 21,181	$ 16,804
Total revenue	12,455	8,615	21,181	16,804
Operating expenses:				
Cost of sales	$ 1,702	$ 1,495	$ 2,787	$ 2,122
Research and development	91,940	77,401	164,683	146,021
Selling, general and administrative	45,869	35,536	87,396	66,550
Total operating expenses	139,511	114,432	254,866	214,693
Loss from operations	(127,056)	(105,817)	(233,685)	(197,889)
Interest income, net	14,513	8,120	30,600	17,009
Other income, net	523	1,579	1,776	3,213
Net loss	$ (112,020)	$ (96,118)	$ (201,309)	$ (177,667)
Net loss per share - basic and diluted	$ (1.93)	$ (1.69)	$ (3.49)	$ (3.14)
Weighted-average number of common shares used in computing net loss per share – basic and diluted	57,932,576	56,802,546	57,697,193	56,593,011

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Comprehensive Loss
(Unaudited)

(In thousands)	Three Months Ended June 30,		Six Months Ended June 30,	
	2025	**2024**	**2025**	**2024**
Net loss	$ (112,020)	$ (96,118)	$ (201,309)	$ (177,667)
Other comprehensive income (loss)				
Unrealized gain (loss) on available-for-sale securities	290	42	2,173	(604)
Comprehensive loss	$ (111,730)	$ (96,076)	$ (199,136)	$ (178,271)

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Stockholders' Equity
(Unaudited)

(in thousands, except share amounts)	Common Stock Shares	Common Stock Amount	Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Treasury Stock Shares	Treasury Stock Amount	Total Stockholders' Equity
Balance at December 31, 2024	73,372,696	$ 73	$ 2,493,811	$ (1,518)	$ (148,924)	(16,216,411)	$ (802,486)	$ 1,540,956
Unrealized gain on available-for-sale securities	—	—	—	1,883	—	—	—	1,883
Common stock issued under stock incentive plan and ESPP	730,496	1	1,618	—	—	—	—	1,619
Stock-based compensation expense	—	—	11,359	—	—	—	—	11,359
Net loss	—	—	—	—	(89,289)	—	—	(89,289)
Balance at March 31, 2025	74,103,192	$ 74	$ 2,506,788	$ 365	$ (238,213)	(16,216,411)	$ (802,486)	$ 1,466,528
Unrealized gain on available-for-sale securities	—	—	—	290	—	—	—	290
Common stock issued under stock incentive plan and ESPP	151,764	—	65	—	—	—	—	65
Stock-based compensation expense	—	—	14,692	—	—	—	—	14,692
Net loss	—	—	—	—	(112,020)	—	—	(112,020)
Balance at June 30, 2025	74,254,956	$ 74	$ 2,521,545	$ 655	$ (350,233)	(16,216,411)	$ (802,486)	$ 1,369,555

(in thousands, except share amounts)	Common Stock Shares	Common Stock Amount	Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Treasury Stock Shares	Treasury Stock Amount	Total Stockholders' Equity
Balance at December 31, 2023	72,161,489	$ 72	$ 2,436,523	$ (441)	$ (822,649)	(16,216,411)	$ (802,486)	$ 811,019
Unrealized loss on available-for-sale securities	—	—	—	(646)	—	—	—	(646)
Common stock issued under stock incentive plan and ESPP	806,433	1	5,863	—	—	—	—	5,864
Stock-based compensation expense	—	—	9,234	—	—	—	—	9,234
Net loss	—	—	—	—	(81,549)	—	—	(81,549)
Balance at March 31, 2024	72,967,922	$ 73	$ 2,451,620	$ (1,087)	$ (904,198)	(16,216,411)	$ (802,486)	$ 743,922
Unrealized gain on available-for-sale securities	—	—	—	42	—	—	—	42
Common stock issued under stock incentive plan and ESPP	123,568	—	1,099	—	—	—	—	1,099
Stock-based compensation expense	—	—	11,565	—	—	—	—	11,565
Net loss	—	—	—	—	(96,118)	—	—	(96,118)
Balance at June 30, 2024	73,091,490	$ 73	$ 2,464,284	$ (1,045)	$ (1,000,316)	(16,216,411)	$ (802,486)	$ 660,510

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Cash Flows
(Unaudited)

(In thousands)	Six Months Ended June 30, 2025	2024
Operating activities		
Net loss	$ (201,309)	$ (177,667)
Adjustments to reconcile net loss from operations to net cash used in operating activities:		
Depreciation and amortization	2,537	2,941
Stock-based compensation expense	26,051	20,799
Net accretion of discount on marketable securities	(3,768)	(5,136)
Loss (gain) on disposal of property and equipment	5	(39)
Non-cash operating lease expense	6,094	5,659
Expense associated with license agreement	10,000	—
Realized gain on investments	(2)	(153)
Changes in operating assets and liabilities:		
Accounts receivable, net	(877)	(952)
Inventory	(3,232)	(4,861)
Prepaid expenses and other current and non-current assets	(3,746)	486
Accounts payable	1,084	268
Accrued expenses and other current liabilities	(11,572)	(6,425)
Income taxes payable	(871)	—
Operating lease liabilities	(8,228)	(7,376)
Other non-current liabilities	(779)	—
Net cash used in operating activities	(188,613)	(172,456)
Investing activities		
Purchases of marketable securities	(305,700)	(348,604)
Proceeds from maturities and sales of marketable securities	508,894	510,669
Payments associated with license agreement	(10,000)	—
Purchases of property and equipment	(1,641)	(299)
Proceeds from sale of equipment	—	40
Net cash provided by investing activities	191,553	161,806
Financing activities		
Net proceeds from stock option exercises and employee stock purchase plan	1,684	6,963
Net cash provided by financing activities	1,684	6,963
Net change in cash and cash equivalents	4,624	(3,687)
Cash and cash equivalents at beginning of the period	76,247	88,205
Cash and cash equivalents at end of the period	$ 80,871	$ 84,518
Supplemental disclosure of non-cash investing and financing transactions		
Additions to property and equipment in accounts payable	$ 122	$ 42
Net cash taxes paid (returned)	$ 1,503	$ (603)

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Notes to Condensed Consolidated Financial Statements
(Unaudited)

1. Overview and Basis of Presentation

References to Agios

Throughout this Quarterly Report on Form 10-Q, "Agios," "the company," "we," "us," and "our," and similar expressions, except where the context requires otherwise, refer to Agios Pharmaceuticals, Inc. and its consolidated subsidiaries, and "our Board of Directors" refers to the board of directors of Agios Pharmaceuticals, Inc.

Overview

We are a biopharmaceutical company committed to transforming patients' lives through leadership in the field of cellular metabolism, with the goal of creating differentiated medicines for rare diseases, with a focus on classical hematology. With a history of focused study on cellular metabolism, we have a deep and mature understanding of this biology, which is involved in the healthy functioning of nearly every system in the body. Building on this expertise, these learnings can be rapidly applied to our clinical trials with the goal of developing medicines that can have a significant impact for patients. We accelerate the impact of our portfolio by cultivating connections with patient communities, healthcare professionals, partners and colleagues to discover, develop and deliver potential therapies for rare diseases. We are located in Cambridge, Massachusetts.

The lead product candidate in our portfolio, PYRUKYND® (mitapivat), is an activator of both wild-type and mutant pyruvate kinase, or PK, enzymes for the potential treatment of hemolytic anemias. PYRUKYND® is approved for use by the U.S. Food and Drug Administration, or FDA, for the treatment of hemolytic anemia in adults with PK deficiency in the United States and by the European Commission for the treatment of PK deficiency in adult patients in the European Union, or EU. Additionally, we received marketing authorization in Great Britain for PYRUKYND® for the treatment of PK deficiency in adult patients under the European Commission Decision Reliance Procedure. In December 2024, we announced that we submitted a supplemental new drug application, or sNDA, to the FDA for PYRUKYND® for the treatment of adult patients with non-transfusion dependent and transfusion-dependent alpha- or beta-thalassemia, which was accepted with standard review by the FDA and granted a Prescription Drug User Fee Act, or PDUFA, goal date of September 7, 2025. Also in December 2024, we announced that we submitted a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, and regulatory applications to the Kingdom of Saudi Arabia and United Arab Emirates health authorities for PYRUKYND® for the treatment of adult patients with non-transfusion dependent and transfusion-dependent alpha- or beta-thalassemia.

In addition, we are currently evaluating PYRUKYND® for the treatment of sickle cell disease, or SCD. We are also developing (i) tebapivat, a novel PK activator, for the potential treatment of lower-risk myelodysplastic syndromes, or LR MDS, and SCD; (ii) AG-181, our phenylalanine hydroxylase, or PAH, stabilizer for the potential treatment of phenylketonuria, or PKU; and (iii) AG-236, an siRNA in-licensed from Alnylam Pharmaceuticals, Inc., or Alnylam, targeting the transmembrane serine protease 6, or TMPRSS6 gene for the potential treatment of polycythemia vera, or PV.

We are subject to risks common to companies in our industry including, but not limited to, uncertainties relating to conducting preclinical and clinical research and development, the manufacture and supply of products for clinical and commercial use, obtaining and maintaining regulatory approvals and pricing and reimbursement for our products, market acceptance, managing global growth and operating expenses, availability of additional capital, competition, obtaining and enforcing patents, stock price volatility, dependence on collaborative relationships and third-party service providers, dependence on key personnel, potential litigation, potential product liability claims and potential government investigations.

Alnylam License Agreement

On July 28, 2023, we entered into a license agreement with Alnylam under which we acquired the rights to develop and commercialize Alnylam's novel preclinical siRNA targeting the TMPRSS6 gene, as a potential disease-modifying treatment for patients with PV.

In accordance with the license agreement, we are responsible to pay up to $130.0 million in potential development and regulatory milestones, in addition to sales milestones as well as tiered royalties on annual net sales, if any, of licensed products, which may be subject to specified reductions and offsets. In the three months ended June 30, 2025, we achieved a regulatory milestone that triggered a $10.0 million payment to Alnylam, which we recorded within research and development expenses in our condensed consolidated statements of operations.

Sale of Oncology Business to Servier and Sale of Contingent Payments

On March 31, 2021, we completed the sale of our oncology business to Servier Pharmaceuticals, LLC, or Servier, which represented a discontinued operation. The transaction included the sale of our oncology business, including TIBSOVO®, our clinical-stage product candidates vorasidenib, AG-270 and AG-636, and our oncology research programs, for a payment of approximately $1.8 billion in cash at the closing, subject to certain adjustments, and a payment of $200.0 million in cash, if, prior to January 1, 2027, vorasidenib is granted new drug application, or NDA, approval from the FDA with an approved label that permits vorasidenib's use as a single agent for the adjuvant treatment of patients with Grade 2 glioma that have an isocitrate dehydrogenase, or IDH, 1 or 2 mutation (and, to the extent required by such approval, the vorasidenib companion diagnostic test is granted an FDA premarket approval), or the Vorasidenib Milestone Payment, as well as a royalty of 5% of U.S. net sales of TIBSOVO® from the close of the transaction through loss of exclusivity, and a royalty of 15% of U.S. net sales of vorasidenib from the first commercial sale of vorasidenib through loss of exclusivity, or the Vorasidenib Royalty Rights. The Vorasidenib Milestone Payment, Vorasidenib Royalty Rights and royalty payments related to TIBSOVO® are referred to as contingent payments and recognized as income when realizable. Servier also acquired our co-commercialization rights for Bristol Myers Squibb's IDHIFA® and the right to receive a $25.0 million potential milestone payment under our prior collaboration agreement with Celgene Corporation, or Celgene, and following the sale Servier has agreed to conduct certain clinical development activities within the IDHIFA® development program.

In October 2022, we sold our rights to future contingent payments associated with the royalty of 5% of U.S. net sales of TIBSOVO® from the close of the transaction through the loss of exclusivity to entities affiliated with Sagard Healthcare Partners, or Sagard, and recognized income of $127.9 million in our consolidated statements of operations for the year ended December 31, 2022.

In August 2024, the FDA approved vorasidenib for adult and pediatric patients 12 years and older with Grade 2 astrocytoma or oligodendroglioma with a susceptible IDH1 or IDH2 mutation, following surgery including biopsy, sub-total resection, or gross total resection. In September 2024, we received the Vorasidenib Milestone Payment from Servier and recognized income of $200.0 million within the milestone payment from gain on sale of oncology business line item in our consolidated statements of operations for the three months ended September 30, 2024. In May 2024, we entered into a purchase and sale agreement to sell the Vorasidenib Royalty Rights to Royalty Pharma Investments 2019 ICAV, or Royalty Pharma, for $905.0 million in cash, or the Upfront Payment. The sale was contingent upon FDA approval of vorasidenib and other customary closing conditions.

Upon consummation of the sale in August 2024, Royalty Pharma acquired 100% of the Vorasidenib Royalty Rights payments made by Servier on account of up to $1.0 billion in U.S. net sales for each calendar year. In addition, any such Vorasidenib Royalty Rights payments made by Servier on account of U.S. net sales in each calendar year in excess of $1.0 billion will be split, with Royalty Pharma having the rights to a 12% earn-out on those excess payments and Agios retaining the rights to a 3% earn-out on those excess payments, or the Retained Earn-Out Rights. As a result of the sale, we recognized income of $889.1 million ($905.0 million net of fees of $15.9 million) within the gain on sale of contingent payments line item in our consolidated statements of operations for the three months ended September 30, 2024. Royalty income related to the Retained Earn-Out Rights, if any, will be recognized in the period when realizable.

Basis of Presentation

The condensed consolidated balance sheet as of June 30, 2025, the condensed consolidated statements of operations, comprehensive loss and stockholders' equity for the three and six months ended June 30, 2025 and 2024, and the condensed consolidated statements of cash flows for the six months ended June 30, 2025 and 2024 are unaudited. The unaudited condensed consolidated financial statements have been prepared on the same basis as the annual financial statements and, in the opinion of our management, reflect all adjustments, which include only normal recurring adjustments, necessary to fairly state our financial position as of June 30, 2025, our results of operations and stockholders' equity for the three and six months ended June 30, 2025 and 2024, and cash flows for the six months ended June 30, 2025 and 2024. The financial data and the other financial information disclosed in these notes to the condensed consolidated financial statements related to the three and six-month periods are also unaudited. The results of operations for the three and six months ended June 30, 2025 are not necessarily indicative of the results to be expected for the year ending December 31, 2025 or for any other future annual or interim period. The condensed consolidated balance sheet data as of December 31, 2024 was derived from our audited financial statements, but does not include all disclosures required by U.S. generally accepted accounting principles, or U.S. GAAP. The condensed consolidated interim financial statements should be read in conjunction with the audited consolidated financial statements and notes thereto included in our Annual Report on Form 10-K for the year ended December 31, 2024 that was filed with the Securities and Exchange Commission, or SEC, on February 13, 2025.

Our condensed consolidated financial statements include our accounts and the accounts of our wholly owned subsidiaries. All intercompany transactions have been eliminated in consolidation. The condensed consolidated financial statements have been prepared in conformity with U.S. GAAP.

Use of Estimates

The preparation of our condensed consolidated financial statements requires us to make estimates, judgments and assumptions that may affect the reported amounts of assets, liabilities, equity, revenues and expenses and related disclosure of contingent assets and liabilities. On an ongoing basis we evaluate our estimates, judgments and methodologies. We base our estimates on historical experience and on various other assumptions that we believe are reasonable, the results of which form the basis for making judgments about the carrying values of assets, liabilities and equity and the amount of revenues and expenses.

Liquidity

As of June 30, 2025, we had cash, cash equivalents and marketable securities of $1.3 billion. Although we have incurred recurring losses and expect to continue to incur losses for the foreseeable future, we expect our cash, cash equivalents and marketable securities to be sufficient to fund current operations for at least the next twelve months from the issuance of the financial statements. If we are unable to raise additional funds through equity or debt financings, we may be required to delay, limit, reduce or terminate product development or future commercialization efforts, or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

2. Summary of Significant Accounting Policies

There have been no material changes to the significant accounting policies previously disclosed in our Annual Report on Form 10-K for the year ended December 31, 2024.

Recent Accounting Pronouncements

Accounting standards that have been issued by the Financial Accounting Standards Board or other standards-setting bodies that do not require adoption until a future date are not expected to have a material impact on our financial statements upon adoption.

3. Fair Value Measurements

We record cash equivalents and marketable securities at fair value. ASC 820, *Fair Value Measurements and Disclosures*, establishes a fair value hierarchy for those instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and our own assumptions (unobservable inputs). The hierarchy consists of three levels:

Level 1 – Unadjusted quoted prices in active markets for identical assets or liabilities.

Level 2 – Quoted prices for similar assets and liabilities in active markets, quoted prices in markets that are not active, or inputs which are observable, directly or indirectly, for substantially the full term of the asset or liability.

Level 3 – Unobservable inputs that reflect our own assumptions about the assumptions market participants would use in pricing the asset or liability in which there is little, if any, market activity for the asset or liability at the measurement date.

The following table summarizes our cash equivalents and marketable securities measured at fair value and by level on a recurring basis as of June 30, 2025:

(In thousands)	Level 1	Level 2	Level 3	Total
Cash equivalents	$ 37,669	$ 16,282	$ —	$ 53,951
Total cash equivalents	37,669	16,282	—	53,951
Marketable securities:				
Certificates of deposit	$ —	$ 7,511	$ —	$ 7,511
U.S. Treasuries	—	264,642	—	264,642
Government securities	—	226,357	—	226,357
Corporate debt securities	—	760,023	—	760,023
Total marketable securities	—	1,258,533	—	1,258,533
Total cash equivalents and marketable securities	$ 37,669	$ 1,274,815	$ —	$ 1,312,484

Cash equivalents and marketable securities have been initially valued at the transaction price and are subsequently valued, at the end of each reporting period, utilizing third-party pricing services or other observable market data. The pricing services utilize industry standard valuation models, including both income and market-based approaches, and observable market inputs to determine value. After completing our validation procedures, we did not adjust or override any fair value measurements provided by the pricing services as of June 30, 2025.

There have been no changes to the valuation methods during the six months ended June 30, 2025, and we had no financial assets or liabilities that were classified as Level 3 at any point during the six months ended June 30, 2025.

4. Marketable Securities

Our marketable securities are classified as available-for-sale pursuant to ASC 320, *Investments – Debt and Equity Securities*, and are recorded at fair value. Unrealized gains and losses are included as a component of accumulated other comprehensive income (loss) in the condensed consolidated balance sheets and statements of stockholders' equity, and a component of total comprehensive income (loss) in the condensed consolidated statements of comprehensive loss, until realized. Unrealized losses are evaluated for impairment under ASC 326, *Financial Instruments - Credit Losses*, to determine if the impairment is credit-related or noncredit-related. Credit-related impairment is recognized as an allowance on the condensed consolidated balance sheets with a corresponding adjustment to earnings, and noncredit-related impairment is recognized in other comprehensive income, net of taxes. Realized gains and losses are included in investment income on a specific-identification basis. There were no material realized gains or losses on marketable securities for the three and six months ended June 30, 2025 or 2024.

Marketable securities at June 30, 2025 consisted of the following:

(In thousands)	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Current:				
Certificates of deposit	$ 7,508	$ 3	$ —	$ 7,511
U.S. Treasuries	144,432	65	(132)	144,365
Government securities	131,602	3	(108)	131,497
Corporate debt securities	574,751	265	(323)	574,693
Total current	858,293	336	(563)	858,066
Non-current:				
U.S. Treasuries	119,706	579	(8)	120,277
Government securities	94,964	28	(132)	94,860
Corporate debt securities	184,915	450	(35)	185,330
Total non-current	399,585	1,057	(175)	400,467
Total marketable securities	$ 1,257,878	$ 1,393	$ (738)	$ 1,258,533

Marketable securities at December 31, 2024 consisted of the following:

(In thousands)	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Current:				
Certificates of deposit	$ 10,374	$ 11	$ —	$ 10,385
U.S. Treasuries	173,465	153	(27)	173,591
Government securities	167,970	103	(75)	167,998
Corporate debt securities	465,427	321	(259)	465,489
Total current	817,236	588	(361)	817,463
Non-current:				
U.S. Treasuries	107,725	106	(303)	107,528
Government securities	112,175	3	(469)	111,709
Corporate debt securities	420,166	181	(1,263)	419,084
Total non-current	640,066	290	(2,035)	638,321
Total marketable securities	$ 1,457,302	$ 878	$ (2,396)	$ 1,455,784

As of June 30, 2025 and December 31, 2024, we held both current and non-current investments. Investments classified as current have maturities of less than one year. Investments classified as non-current are those that: (i) have a maturity of greater

than one year, and (ii) we do not intend to liquidate within the next twelve months, although these funds are available for use and, therefore, are classified as available-for-sale.

As of June 30, 2025 and December 31, 2024, we held 123 and 213 debt securities, respectively, that were in an unrealized loss position for less than one year. We did not record an allowance for credit losses as of June 30, 2025 and December 31, 2024 related to these securities. The aggregate fair value of debt securities in an unrealized loss position at June 30, 2025 and December 31, 2024 was $626.8 million and $768.1 million, respectively. There were no individual securities that were in a significant unrealized loss position as of June 30, 2025 and December 31, 2024. We regularly review the securities in an unrealized loss position and evaluate the current expected credit loss by considering factors such as historical experience, market data, issuer-specific factors, and current economic conditions. We do not consider these marketable securities to be impaired as of June 30, 2025 and December 31, 2024.

5. Inventory

Inventory, which consists of commercial supply of PYRUKYND®, consisted of the following:

(In thousands)	June 30, 2025	December 31, 2024
Raw materials	$ 89	$ 89
Work-in-process	27,207	24,509
Finished goods	3,552	3,018
Total inventory	$ 30,848	$ 27,616

6. Leases

Our building leases are comprised of office and laboratory space under non-cancelable operating leases. These lease agreements have remaining lease terms of approximately three years and contain various clauses for renewal at our option. The renewal options were not included in the calculation of the operating lease assets and the operating lease liabilities as the renewal options are not reasonably certain of being exercised. The lease agreements do not contain residual value guarantees.

The components of lease expense and other information related to leases were as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2025	2024	2025	2024
Operating lease costs	$ 3,806	$ 3,806	$ 7,613	$ 7,613
Cash paid for amounts included in the measurement of operating lease liabilities	4,911	4,678	9,748	9,331

We have not entered into any material short-term leases or financing leases as of June 30, 2025.

In arriving at the operating lease liabilities as of June 30, 2025 and December 31, 2024, we applied the weighted-average incremental borrowing rate of 5.7% for both periods over a weighted-average remaining lease term of 2.7 and 3.2 years, respectively.

As of June 30, 2025, undiscounted minimum rental commitments under non-cancelable leases were as follows:

(In thousands)	
Remaining 2025	$ 8,195
2026	20,151
2027	20,755
2028	3,479
Undiscounted minimum rental commitments	$ 52,580
Interest	(3,820)
Operating lease liabilities	$ 48,760

We provided our landlord a security deposit of $2.9 million as security for our leases, which is included within other non-current assets on our condensed consolidated balance sheet.

In August 2021, we entered into a long-term sublease agreement for 13,000 square feet of the office space at 38 Sidney Street, Cambridge, Massachusetts, which expired on December 31, 2024. In April 2022, we entered into a long-term sublease agreement for 27,000 square feet of the office space at 64 Sidney Street, Cambridge, Massachusetts, which expired on April 30, 2025.

In May 2023, we entered into a long-term sublease agreement for 7,407 square feet of office space on the first floor of 64 Sidney Street, Cambridge, Massachusetts, which expired on July 31, 2025. In July 2025, we entered into a long-term sublease agreement with a new tenant for the same space, which will begin in November 2025 with the term of the lease running through February 2028.

We recorded operating sublease income of $0.5 million and $1.6 million for the three months ended June 30, 2025 and 2024, respectively, and $1.8 million and $3.2 million for the six months ended June 30, 2025 and 2024, respectively, in other income, net in the condensed consolidated statements of operations. We hold security deposits from our sublessee of approximately $0.1 million which is recorded within other non-current assets on our condensed consolidated balance sheet.

As of June 30, 2025, the future minimum lease payments to be received under the long-term sublease agreements were as follows:

(In thousands)	
Remaining 2025	$ 31
Total	$ 31

7. Accrued Expenses

Accrued expenses consisted of the following:

(In thousands)	June 30, 2025	December 31, 2024
Accrued compensation	$ 15,323	$ 29,935
Accrued research and development costs	13,065	10,548
Accrued professional fees	3,153	4,316
Accrued other	3,748	2,062
Total accrued expenses	$ 35,289	$ 46,861

8. Product Revenue

We generate product revenue from sales of PYRUKYND® to a limited number of specialty distributors and specialty pharmacy providers, or collectively, the Customers. These Customers subsequently resell PYRUKYND® to pharmacies or dispense PYRUKYND® directly to patients. In addition to distribution agreements with Customers, we enter into arrangements with healthcare providers and payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks and discounts with respect to the purchase of PYRUKYND®.

The performance obligation related to the sale of PYRUKYND® is satisfied and revenue is recognized when the Customer obtains control of the product, which occurs at a point in time, typically upon delivery to the Customer.

Product revenue, net, were as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2025	2024	2025	2024
Product revenue, net	$ 12,455	$ 8,615	$ 21,181	$ 16,804

Reserves for Variable Consideration

Revenues from product sales are recorded at the net sales price, or transaction price, which includes estimates of variable consideration for which reserves are established and result from contractual adjustments, government rebates, returns and other allowances that are offered within the contracts with our Customers, healthcare providers, payors and other indirect customers relating to the sale of our products.

Contractual Adjustments

We generally provide Customers with discounts, including prompt pay discounts, and allowances that are explicitly stated in the contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, we receive sales order management, data and distribution services from certain Customers.

Chargebacks and discounts represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to Customers who directly purchase the product from us. Customers charge us for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. These reserves are estimated using the expected value method, based upon a range of possible outcomes that are probability-weighted for the estimated channel mix and are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue.

Government Rebates

Government rebates include Medicare, TriCare, and Medicaid rebates, which we estimate using the expected value method, based upon a range of possible outcomes that are probability-weighted for the estimated payor mix. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue. For Medicare, we also estimate the number of patients for whom we will owe an additional liability under the Medicare Part D Manufacturer Discount Program.

Returns / Replacement

We estimate the amount of product sales that may be returned by Customers or replaced by Agios and record this estimate as a reduction of revenue in the period the related product revenue is recognized. We currently estimate product return and replacement liabilities using the expected value method, based on available industry data, including our visibility into the inventory remaining in the distribution channel.

The following table summarizes balances and activity in each of the product revenue allowance and reserve categories for the six months ended June 30, 2025:

(In thousands)	Contractual Adjustments	Government Rebates	Returns/ Replacement	Total
Balance at December 31, 2024	$ 253	$ 1,354	$ 489	$ 2,096
Current provisions relating to sales in the current year	733	1,298	256	2,287
Adjustments relating to prior years	(51)	(83)	—	(134)
Payments/returns relating to sales in the current year	(610)	(428)	—	(1,038)
Payments/returns relating to sales in the prior years	(202)	(462)	—	(664)
Balance at June 30, 2025	$ 123	$ 1,679	$ 745	$ 2,547

Total revenue-related reserves above, included in our condensed consolidated balance sheets, are summarized as follows:

(In thousands)	June 30, 2025	December 31, 2024
Reduction of accounts receivable	$ 104	$ 124
Component of accrued expenses	2,443	1,972
Total revenue-related reserves	$ 2,547	$ 2,096

The following table presents changes in our contract assets during the six months ended June 30, 2025:

(In thousands)	December 31, 2024	Additions	Deductions	June 30, 2025
Contract assets[1]				
Accounts receivable, net	$ 4,109	$ 23,333	$ (22,456)	$ 4,986

(1) Additions to contract assets relate to amounts billed to Customers for product sales and deductions to contract assets primarily relate to collection of receivables during the reporting period.

9. Share-Based Payments

2023 Stock Incentive Plan and Inducement Grants

In June 2023, our stockholders approved the 2023 Stock Incentive Plan, or the 2023 Plan. The 2023 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units, or RSUs, performance-based share units, or PSUs, and other stock-based awards to employees, advisors, consultants and non-employee directors.

Following the adoption of the 2023 Plan, we ceased granting equity awards under the 2013 Stock Incentive Plan, or the 2013 Plan. Any outstanding equity awards that were previously granted under the 2013 Plan continue to be governed by their terms. Following adoption of the 2013 Plan, we ceased granting equity awards under the 2007 Stock Incentive Plan, or the 2007 Plan. There are no outstanding equity awards under the 2007 Plan.

In connection with the start of employment of our Chief Executive Officer and Chief Financial Officer in 2022, our Chief Commercial Officer in 2023, and our Chief Corporate Development and Strategy Officer in March 2025, our Board of Directors granted each of them equity awards in the form of stock options, RSUs and PSUs, which awards were made outside our equity incentive plans as inducements material to their respective entry into employment with us in accordance with Nasdaq Listing Rule 5635(c)(4).

As of June 30, 2025, the maximum number of shares reserved under the 2013 Plan, the 2023 Plan and the inducement grants described above was 12,661,855, and we had 3,664,151 shares available for future issuance under the 2023 Plan.

Stock options

The following table presents stock option activity for the six months ended June 30, 2025:

	Number of Stock Options		Weighted-Average Exercise Price
Outstanding at December 31, 2024	5,834,256	$	43.48
Granted	885,023		33.40
Exercised	(3,783)		29.10
Cancelled/Forfeited	(80,385)		45.29
Expired	(210,536)		106.49
Outstanding at June 30, 2025	6,424,575	$	40.01
Exercisable at June 30, 2025	4,243,623	$	44.21
Vested and expected to vest at June 30, 2025	6,424,575	$	40.01

At June 30, 2025, there was approximately $35.8 million of total unrecognized compensation expense related to unvested stock option awards, which we expect to recognize over a weighted-average period of approximately 2.57 years.

Restricted stock units

The following table presents RSU activity for the six months ended June 30, 2025:

	Number of Stock Units		Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2024	1,818,563	$	30.31
Granted	1,114,325		33.16
Vested	(743,358)		30.06
Forfeited	(93,407)		30.56
Unvested shares at June 30, 2025	2,096,123	$	31.90

As of June 30, 2025, there was approximately $53.6 million of total unrecognized compensation expense related to RSUs, which we expect to recognize over a weighted-average period of approximately 2.10 years.

Performance-based stock units

The following table presents PSU activity for the six months ended June 30, 2025:

	Number of Stock Units	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2024	374,583	$ 29.45
Granted	185,450	33.25
Vested	(83,027)	26.35
Unvested shares at June 30, 2025	477,006	$ 31.47

Stock-based compensation expense associated with these PSUs is recognized if the underlying performance condition is considered probable of achievement using our management's best estimates.

As of June 30, 2025, there was no unrecognized compensation expense related to PSUs with performance-based vesting criteria that are considered probable of achievement, and $15.0 million of total unrecognized compensation expense related to PSUs with performance-based vesting criteria that are considered not probable of achievement.

2013 Employee Stock Purchase Plan

In June 2013, our Board of Directors adopted, and in July 2013 our stockholders approved, the 2013 Employee Stock Purchase Plan, or the 2013 ESPP. We issued and sold 52,092 and 52,514 shares of common stock during the six months ended June 30, 2025 and 2024, respectively, under the 2013 ESPP. The 2013 ESPP provides participating employees with the opportunity to purchase up to an aggregate of 2,363,636 shares of our common stock. As of June 30, 2025, we had 1,531,142 shares of common stock available for future issuance under the 2013 ESPP.

Stock-based compensation expense

Stock-based compensation expense by award type included within the condensed consolidated statements of operations is as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2025	2024	2025	2024
Stock options	$ 4,622	$ 4,361	$ 9,022	$ 8,432
Restricted stock units	7,507	6,211	14,191	11,177
Performance-based stock units	2,188	750	2,188	750
Employee stock purchase plan	375	243	650	440
Total stock-based compensation expense	$ 14,692	$ 11,565	$ 26,051	$ 20,799

Expenses related to stock options and stock-based awards were allocated as follows in the condensed consolidated statements of operations:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2025	2024	2025	2024
Research and development expense	$ 5,336	$ 4,460	$ 9,940	$ 8,235
Selling, general and administrative expense	9,356	7,105	16,111	12,564
Total stock-based compensation expense	$ 14,692	$ 11,565	$ 26,051	$ 20,799

10. Loss per Share

Basic net income (loss) per share is calculated by dividing net income (loss) by the weighted-average shares outstanding during the period, without consideration for common stock equivalents. Diluted net income (loss) per share is calculated by adjusting the weighted-average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury stock method. For purposes of the dilutive net income (loss) per share calculation, stock options, RSUs and PSUs for which the performance and market vesting conditions, respectively, have been deemed probable, and 2013 ESPP shares are considered to be common stock equivalents, while PSUs with performance and market vesting conditions, respectively, that were not deemed probable as of June 30, 2025 are not considered to be common stock equivalents.

We utilize the control number concept in the computation of diluted earnings per share to determine whether potential common stock equivalents are dilutive. The control number used is net loss from continuing operations. The control number concept requires that the same number of potentially dilutive securities applied in computing diluted earnings per share from continuing operations be applied to all other categories of income or loss, regardless of their anti-dilutive effect on such categories. Since we had a net loss for all periods presented, no dilutive effect has been recognized in the calculation of loss per share. Basic and diluted net loss per share was the same for all periods presented.

The following common stock equivalents were excluded from the calculation of diluted net loss per share applicable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	Three Months Ended June 30,	
	2025	2024
Stock options	6,424,575	5,996,025
Restricted stock units	2,096,123	1,860,408
Employee stock purchase plan shares	45,571	39,381
Total common stock equivalents	8,566,269	7,895,814

11. Segment Information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or CODM, or decision-making group in making decisions on how to allocate resources and assess performance. Our CODM is our CEO. Our CEO views our operations and manages our business as one operating segment, which derives its revenues from the development and commercialization of therapies for patients with rare diseases.

Our CEO manages and allocates resources to the operations of our company on a total company basis by assessing the overall level of resources available and how to best deploy these resources across functions and research and development projects that are in line with our long-term company-wide strategic goals. In making these decisions, our CEO uses consolidated financial information for purposes of evaluating performance, forecasting future period financial results, allocating resources and setting incentive targets. The CODM performs this assessment based on our consolidated net income (loss). Through this analysis, the CODM assesses performance by comparing actual consolidated net income (loss) versus the budget, and then decides how to allocate resources to invest in our research and development programs. The measure of segment assets is reported on the condensed consolidated balance sheets as total assets.

The following table contains additional information on our consolidated revenue and net loss, including significant segment expenses:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2025	2024	2025	2024
Product revenue, net	$ 12,455	$ 8,615	$ 21,181	$ 16,804
PK activator (PYRUKYND®) direct expenses - research and development	(29,809)	(27,968)	(51,130)	(54,004)
Compensation and related expenses - research and development	(27,594)	(27,476)	(60,584)	(55,110)
Total selling, general and administrative expenses	(45,869)	(35,536)	(87,396)	(66,550)
Other segment items*	(21,203)	(13,753)	(23,380)	(18,807)
Net loss	$ (112,020)	$ (96,118)	$ (201,309)	$ (177,667)

*Other segment items primarily include cost of sales, other research and development expenses and interest income.

12. Subsequent Events

On July 4, 2025, the One Big Beautiful Bill Act, or OBBBA, was enacted in the United States, which includes significant changes to federal tax law and other regulatory provisions that may impact the Company. We are currently evaluating the impact of the OBBBA on our financial condition and results of operations.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

Forward-looking Information

The following discussion of our financial condition and results of operations should be read in conjunction with our unaudited condensed consolidated financial statements as of June 30, 2025 and for the three and six months ended June 30, 2025 and 2024, and related notes included in Part I, Item 1 of this Quarterly Report on Form 10-Q, as well as the audited consolidated financial statements and notes and Management's Discussion and Analysis of Financial Condition and Results of Operations, included in our Annual Report on Form 10-K for the year ended December 31, 2024 filed with the SEC on February 13, 2025. This Management's Discussion and Analysis of Financial Condition and Results of Operations contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on current expectations, estimates, forecasts and projections, and the beliefs and assumptions of our management, and include, without limitation, statements with respect to our expectations regarding our research, development and commercialization plans and prospects, results of operations, selling, general and administrative expenses, research and development expenses, and the sufficiency of our cash for future operations. Words such as "aim," "anticipate," "believe," "continue," "could," "estimate," "expect," "goal," "intend," "may," "might," "plan," "potential," "predict," "project," "should," "strategy," "target," "vision," "will," "would" or the negatives of these words and similar expressions are intended to identify these forward-looking statements, although not all forward-looking statements contain these identifying words. Readers are cautioned that these forward-looking statements are predictions and are subject to risks, uncertainties and assumptions that are difficult to predict. Therefore, actual results may differ materially and adversely from those expressed in any forward-looking statements. Among the important factors that could cause actual results to differ materially from those indicated by our forward-looking statements are those discussed under the heading "Risk Factors" in Part II, Item 1A and elsewhere in this report, and in our Annual Report on Form 10-K for the year ended December 31, 2024. We undertake no obligation to revise the forward-looking statements contained herein to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events, except as required by law.

Overview

We are a biopharmaceutical company committed to transforming patients' lives through leadership in the field of cellular metabolism, with the goal of creating differentiated medicines for rare diseases, with a focus on classical hematology. With a history of focused study on cellular metabolism, we have a deep and mature understanding of this biology, which is involved in the healthy functioning of nearly every system in the body. Building on this expertise, these learnings can be rapidly applied to our clinical trials with the goal of developing medicines that can have a significant impact for patients. We accelerate the impact of our portfolio by cultivating connections with patient communities, healthcare professionals, partners and colleagues to discover, develop and deliver potential therapies for rare diseases.

The lead product candidate in our portfolio, PYRUKYND® (mitapivat), is an activator of both wild-type and mutant pyruvate kinase, or PK, enzymes for the potential treatment of hemolytic anemias. PYRUKYND® is approved for use by the U.S. Food and Drug Administration, or FDA, for the treatment of hemolytic anemia in adults with PK deficiency in the United States and by the European Commission for the treatment of PK deficiency in adult patients in the European Union, or EU. Additionally, we received marketing authorization in Great Britain for PYRUKYND® for the treatment of PK deficiency in adult patients under the European Commission Decision Reliance Procedure. In December 2024, we announced that we submitted a supplemental new drug application, or sNDA, to the FDA for PYRUKYND® for the treatment of adult patients with non-transfusion dependent and transfusion-dependent alpha- or beta-thalassemia, which was accepted with standard review by the FDA and granted a Prescription Drug User Fee Act, or PDUFA, goal date of September 7, 2025. Also in December 2024, we announced that we submitted a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, and regulatory applications to the Kingdom of Saudi Arabia and United Arab Emirates health authorities for PYRUKYND® for the treatment of adult patients with non-transfusion dependent and transfusion-dependent alpha- or beta-thalassemia.

In addition, we are currently evaluating PYRUKYND® for the treatment of sickle cell disease, or SCD. We are also developing (i) tebapivat, a novel PK activator, for the potential treatment of lower-risk myelodysplastic syndromes, or LR MDS, and SCD; (ii) AG-181, our phenylalanine hydroxylase, or PAH, stabilizer for the potential treatment of phenylketonuria, or PKU; and (iii) AG-236, an siRNA in-licensed from Alnylam Pharmaceuticals, Inc., or Alnylam, targeting the transmembrane serine protease 6, or TMPRSS6 gene for the potential treatment of polycythemia vera, or PV.

Alnylam License Agreement

On July 28, 2023, we entered into a license agreement with Alnylam under which we acquired the rights to develop and commercialize Alnylam's novel preclinical siRNA targeting the TMPRSS6 gene, as a potential disease-modifying treatment for patients with PV.

In accordance with the license agreement, we are responsible to pay up to $130.0 million in potential development and regulatory milestones, in addition to sales milestones as well as tiered royalties on annual net sales, if any, of licensed products, which may be subject to specified reductions and offsets. In the three months ended June 30, 2025, we achieved a regulatory milestone that triggered a $10.0 million payment to Alnylam, which we recorded within research and development expenses in our condensed consolidated statements of operations.

Sale of Oncology Business to Servier and Sale of Contingent Payments

On March 31, 2021, we completed the sale of our oncology business to Servier Pharmaceuticals, LLC, or Servier, which represented a discontinued operation. The transaction included the sale of our oncology business, including TIBSOVO®, our clinical-stage product candidates vorasidenib, AG-270 and AG-636, and our oncology research programs, for a payment of approximately $1.8 billion in cash at the closing, subject to certain adjustments, and a payment of $200.0 million in cash, if, prior to January 1, 2027, vorasidenib is granted new drug application, or NDA, approval from the FDA with an approved label that permits vorasidenib's use as a single agent for the adjuvant treatment of patients with Grade 2 glioma that have an isocitrate dehydrogenase, or IDH, 1 or 2 mutation (and, to the extent required by such approval, the vorasidenib companion diagnostic test is granted an FDA premarket approval), or the Vorasidenib Milestone Payment, as well as a royalty of 5% of U.S. net sales of TIBSOVO® from the close of the transaction through loss of exclusivity, and a royalty of 15% of U.S. net sales of vorasidenib from the first commercial sale of vorasidenib through loss of exclusivity, or the Vorasidenib Royalty Rights. The Vorasidenib Milestone Payment, Vorasidenib Royalty Rights and royalty payments related to TIBSOVO® are referred to as contingent payments and recognized as income when realizable. Servier also acquired our co-commercialization rights for Bristol Myers Squibb's IDHIFA® and the right to receive a $25.0 million potential milestone payment under our prior collaboration agreement with Celgene Corporation, or Celgene, and following the sale Servier has agreed to conduct certain clinical development activities within the IDHIFA® development program.

In October 2022, we sold our rights to future contingent payments associated with the royalty of 5% of U.S. net sales of TIBSOVO® from the close of the transaction through the loss of exclusivity to entities affiliated with Sagard Healthcare Partners, or Sagard, and recognized income of $127.9 million in our consolidated statements of operations for the year ended December 31, 2022.

In August 2024, the FDA approved vorasidenib for adult and pediatric patients 12 years and older with Grade 2 astrocytoma or oligodendroglioma with a susceptible IDH1 or IDH2 mutation, following surgery including biopsy, sub-total resection, or gross total resection. In September 2024, we received the Vorasidenib Milestone Payment from Servier and recognized income of $200.0 million within the milestone payment from gain on sale of oncology business line item in our consolidated statements of operations for the three months ended September 30, 2024. In May 2024, we entered into a purchase and sale agreement to sell the Vorasidenib Royalty Rights to Royalty Pharma Investments 2019 ICAV, or Royalty Pharma, for $905.0 million in cash, or the Upfront Payment. The sale was contingent upon FDA approval of vorasidenib and other customary closing conditions.

Upon consummation of the sale in August 2024, Royalty Pharma acquired 100% of the Vorasidenib Royalty Rights payments made by Servier on account of up to $1.0 billion in U.S. net sales for each calendar year. In addition, any such Vorasidenib Royalty Rights payments made by Servier on account of U.S. net sales in each calendar year in excess of $1.0 billion will be split, with Royalty Pharma having the rights to a 12% earn-out on those excess payments and Agios retaining the rights to a 3% earn-out on those excess payments, or the Retained Earn-Out Rights. As a result of the sale, we recognized income of $889.1 million ($905.0 million net of fees of $15.9 million) within the gain on sale of contingent payments line item in our consolidated statements of operations for the three months ended September 30, 2024. Royalty income related to the Retained Earn-Out Rights, if any, will be recognized in the period when realizable.

Financial Operations Overview

General

Since inception, our operations have primarily focused on organizing and staffing our company, business planning, raising capital, assembling our core capabilities in cellular metabolism and classical hematology, identifying potential product candidates, undertaking preclinical studies, conducting clinical trials, establishing a commercial infrastructure, preparing for and executing on the commercial launch of PYRUKYND® and, prior to the sale of our oncology business to Servier on March 31, 2021, marketing TIBSOVO® and IDHIFA®. Through March 31, 2021, we financed our operations primarily through proceeds from the sale of our royalty rights, commercial sales of TIBSOVO®, funding received from our collaboration

agreements, private placements of our preferred stock, our initial public offering of our common stock and concurrent private placement of common stock to an affiliate of Celgene, and our follow-on public offerings. Following the sale of our oncology business to Servier on March 31, 2021, we have financed and expect to continue to finance our operations primarily through cash on hand, potential royalty payments with respect to the Retained Earn-Out Rights, the actual and potential future sales of PYRUKYND® and, potentially, collaborations, strategic alliances, licensing arrangements and other nondilutive strategic transactions. In addition, we may pursue opportunistic debt offerings, and equity or equity-linked offerings.

Additionally, since inception, we have historically incurred significant operating losses. Our net loss for the six months ended June 30, 2025 was $201.3 million and our net loss for the six months ended June 30, 2024 was $177.7 million. As of June 30, 2025, we had an accumulated deficit of $350.2 million. We expect to continue to incur significant expenses and net losses until such time we are able to report profitable results. Our net losses may fluctuate significantly from year to year. We expect that we will continue to incur significant expenses as we continue to advance and expand clinical development and commercialization activities for PYRUKYND®, including with respect to the review by the FDA and other regulatory authorities of our regulatory submissions made for the treatment of thalassemia, which we announced in December 2024; continue to advance and expand clinical development of tebapivat, our novel PK activator; continue to advance clinical development of AG-181, our PAH stabilizer; continue clinical development of AG-236, a licensed siRNA development candidate pursuant to our license agreement with Alnylam; expand and protect our intellectual property portfolio, including by in-licensing or acquiring assets for pipeline growth; and hire additional commercial and development personnel.

Revenues

Our wholly owned product, PYRUKYND®, received approval from the FDA on February 17, 2022, for the treatment of hemolytic anemia in adults with PK deficiency in the United States. Upon FDA approval of PYRUKYND® in the United States, we began generating product revenue from sales of PYRUKYND®. We sell PYRUKYND® to a limited number of specialty distributors and specialty pharmacy providers, or collectively, the Customers. These Customers subsequently resell PYRUKYND® to pharmacies or dispense PYRUKYND® directly to patients. In addition to distribution agreements with Customers, we enter into arrangements with healthcare providers and payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks and discounts with respect to the purchase of PYRUKYND®.

In July 2024, we entered into a distribution agreement, or the NewBridge Agreement, with NewBridge Pharmaceuticals FZ-LLC, or NewBridge, pursuant to which we granted NewBridge the right to commercialize PYRUKYND® in Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and the United Arab Emirates, or the Gulf Cooperation Council region. In June 2025, we entered into a distribution agreement, or the Avanzanite Agreement, with Avanzanite Bioscience B.V., or Avanzanite, pursuant to which we granted Avanzanite the right to commercialize PYRUKYND® in the European Economic Area, Switzerland, and the U.K. For further discussion of our revenue recognition policy, see Note 8, *Product Revenue*, to the condensed consolidated financial statements in this Quarterly Report on Form 10-Q.

In the future, we expect to continue to generate revenue from product sales. We may also generate revenue from milestone payments, upfront payments or royalties on product sales under collaborations or licensing agreements that we may enter into in the future.

Cost of Sales

Cost of sales consists primarily of manufacturing costs for sales of PYRUKYND®. Based on our policy to expense costs associated with the manufacturing of our products prior to regulatory approval, certain of the manufacturing costs associated with product shipments of PYRUKYND® recorded during the three and six months ended June 30, 2025 and 2024 were expensed prior to February 17, 2022, and, therefore, are not included in costs of sales during the three and six months ended June 30, 2025 and 2024. The amounts excluded from cost of sales were not significant during the three and six months ended June 30, 2025 and 2024.

Inventories are reviewed periodically to identify excess or obsolete inventory based on projected sales activity as well as product shelf-life. Expired inventory is disposed of, and the related costs are recognized as cost of sales in our consolidated statements of operations, when, based on the expiry date, we do not believe we are able to sell the inventory. We have not reserved for excess or obsolete inventory during the three and six months ended June 30, 2025 and 2024.

Research and Development Expenses

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect research and development costs related to our portfolio to increase as our product candidate development programs progress. However, the successful development of our product candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of and to commercialize these product candidates. We

are unable to predict the amount of net cash inflows from PYRUKYND® or any of our product candidates. This is due to the numerous risks and uncertainties associated with developing medicines, including the uncertainty of:

- establishing an appropriate safety profile with an investigational new drug application, or IND, and/or NDA-enabling toxicology and clinical trials;
- successfully enrolling in, and completion of, clinical trials;
- receiving marketing approvals from applicable regulatory authorities;
- establishing compliant commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- launching commercial sales of the products, if and when approved, in the United States or in other jurisdictions, whether alone or in collaboration with others, including pursuant to the NewBridge Agreement and Avanzanite Agreement; and
- maintaining an acceptable safety profile of the products following approval.

A change in the outcome of any of these variables with respect to the development of any of our product candidates would significantly change the costs and timing associated with the development of that product candidate.

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts, and the development of our product candidates, which include:

- employee-related expenses, including salaries, benefits and stock-based compensation expense;
- expenses incurred under agreements with third parties, including contract research organizations, or CROs, that conduct research and development and both preclinical and clinical activities on our behalf, and the cost of consultants;
- the cost of lab supplies and acquiring, developing and manufacturing preclinical study and clinical trial materials; and
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and the maintenance of facilities, insurance and other operating costs.

The following summarizes our most advanced programs:

PYRUKYND® (mitapivat): First-in-Class PK Activator

We are developing PYRUKYND® for the treatment of PK deficiency and other hemolytic anemias such as thalassemia and SCD. PYRUKYND® is an orally available small molecule and a potent activator of the wild-type and mutated PK enzymes.

PYRUKYND® is approved for use by the FDA for the treatment of hemolytic anemia in adults with PK deficiency in the United States and by the European Commission for the treatment of PK deficiency in adult patients in the EU. Additionally, we received marketing authorization in Great Britain for PYRUKYND® for the treatment of PK deficiency in adult patients under the European Commission Decision Reliance Procedure. In December 2024, we announced that we submitted an sNDA to the FDA for PYRUKYND® for the treatment of adult patients with non-transfusion dependent and transfusion-dependent alpha- or beta-thalassemia, which was accepted with standard review by the FDA and granted a PDUFA goal date of September 7, 2025. Also in December 2024, we announced that we submitted an MAA to the EMA and regulatory applications to the Kingdom of Saudi Arabia and United Arab Emirates health authorities for PYRUKYND® for the treatment of adult patients with non-transfusion dependent and transfusion-dependent alpha- or beta-thalassemia. In addition, we are currently evaluating PYRUKYND® in clinical trials for the treatment of SCD and in pediatric patients with PK deficiency.

We have full ownership rights to PYRUKYND® and expect to fund the future development and commercialization costs related to PYRUKYND®. In July 2024, we entered into a distribution agreement with NewBridge Pharmaceuticals FZ-LLC, or the NewBridge Agreement, pursuant to which we granted NewBridge the right to commercialize PYRUKYND® in the Gulf Cooperation Council region. In June 2025, we entered into a distribution agreement with Avanzanite Bioscience B.V., or the Avanzanite Agreement, pursuant to which we granted Avanzanite the right to commercialize PYRUKYND® in the European Economic Area, Switzerland, and the U.K. PYRUKYND® has been granted orphan drug designation for the treatment of PK deficiency by the FDA and the EMA. Additionally, PYRUKYND® has received orphan drug designation from the FDA for the treatment of thalassemia and SCD, orphan medicinal product designation from the EMA for the treatment of SCD, and breakthrough medicine designation from the Saudi Food and Drug Authority for the treatment of thalassemia.

We built our commercial infrastructure to support the commercialization of PYRUKYND® in adult PK deficiency in the United States, and have expanded this infrastructure to support the potential commercial launch of PYRUKYND® in thalassemia in the United States. In connection with our regulatory approvals in the EU and Great Britain, we are currently providing access to PYRUKYND® on either a free of charge or for charge basis for eligible patients in those jurisdictions through a global managed access program. We provide access to PYRUKYND® for adult patients with PK deficiency in other jurisdictions upon request through the global managed access program, on either a free of charge or for charge basis. Our global managed access program has not had a significant impact on our business, financial condition or results of operations. Beyond the global managed access program, we have entered into the NewBridge Agreement and the Avanzanite Agreement for commercialization of PYRUKYND® in certain regions outside of the United States and we continue to evaluate other options for the commercialization of PYRUKYND® outside of the United States, including through exploring potential partnership opportunities.

We are evaluating PYRUKYND® in numerous clinical trials, including the following:

- An extension study evaluating the long-term safety, tolerability and efficacy of treatment with PYRUKYND® in patients from ENERGIZE, our completed phase 3, double-blind, randomized, placebo-controlled multicenter study pivotal trial of PYRUKYND® in adults with non-transfusion-dependent alpha- or beta-thalassemia. We announced topline data for ENERGIZE in January 2024 and a more detailed analysis of the data in June 2024. A total of 194 patients were enrolled in the study, with 130 randomized to PYRUKYND® 100 mg twice-daily, or BID, and 64 randomized to matched placebo. 122 patients (93.8%) in the PYRUKYND® arm and 62 patients (96.9%) in the placebo arm completed the 24-week double-blind period of the study. The study met the primary endpoint of hemoglobin response, where treatment with PYRUKYND® demonstrated a statistically significant increase in hemoglobin response compared to placebo, as 42.3% of patients in the PYRUKYND® arm achieved a hemoglobin response, compared to 1.6% of patients in the placebo arm (2-sided $p<0.0001$). Treatment with PYRUKYND® also demonstrated statistically significant improvements compared to placebo for both key secondary endpoints: (i) change from baseline in average Functional Assessment of Chronic Illness Therapy-Fatigue, or FACIT-Fatigue, subscale score from week 12 to week 24 and (ii) change from baseline in average hemoglobin concentration from week 12 to week 24. During the 24-week double-blind period, four (3.1%) subjects in the PYRUKYND® arm experienced adverse events, or AEs, leading to discontinuation, and there were no AEs in the placebo arm leading to discontinuation. AEs that led to discontinuation in the PYRUKYND® arm were thrombocytopenia, arthralgia, abdominal distension, and 5 concurrent laboratory adverse events (alanine aminotransferase increase, aspartate aminotransferase increase, blood bilirubin increase, blood LDH increase, and international normalized ratio increase), all in one patient each.
- An extension study evaluating the long-term safety, tolerability and efficacy of treatment with PYRUKYND® in patients from ENERGIZE-T, our completed phase 3, double-blind, randomized, placebo-controlled multicenter study evaluating the efficacy and safety of PYRUKYND® as a potential treatment for adults with transfusion-dependent alpha- or beta-thalassemia, defined as 6 to 20 red blood cell, or RBC, units transfused and ≤ six-week transfusion-free period during the 24-week period before randomization. The primary endpoint of the trial is percentage of patients with transfusion reduction response, defined as a ≥50% reduction in transfused RBC units with a reduction of ≥2 units of transfused RBCs in any consecutive 12-week period through week 48 compared with baseline. Secondary endpoints include additional transfusion reduction measures and percentage of participants with transfusion-independence. We announced topline data for ENERGIZE-T in June 2024 and a more detailed analysis of the data in December 2024. A total of 258 patients were enrolled in the study, with 171 randomized to PYRUKYND® 100 mg twice-daily and 87 randomized to matched placebo. 155 patients (90.6%) in the PYRUKYND® arm and 83 patients (95.4%) in the placebo arm completed the 48-week double-blind period of the study. The study met the primary endpoint of transfusion reduction response, where treatment with PYRUKYND® demonstrated a statistically significant reduction in transfusion burden compared to placebo, as 30.4% of patients achieved a transfusion reduction response, compared to 12.6% of patients in the placebo arm (2-sided $p=0.0003$). Treatment with PYRUKYND® also demonstrated a statistically significant reduction in additional measures of transfusion reduction response compared to placebo as assessed by the three key secondary endpoints: (i) ≥50% reduction in transfused RBC units in any consecutive 24-week period through week 48 compared with baseline, (ii) ≥33% reduction in transfused RBC units from week 13 through week 48 compared with baseline, and (iii) ≥50% reduction in transfused RBC units from week 13 through week 48 compared with baseline. In addition, a higher proportion of patients in the PYRUKYND® arm (9.9%) compared to the placebo arm (1.1%) achieved the secondary endpoint of transfusion independence (transfusion-free for ≥8 consecutive weeks through week 48). The proportion of patients with any treatment-emergent adverse events, or TEAEs, was 90.1% in patients on PYRUKYND® and 83.5% in patients on placebo. The most frequent TEAEs that occurred in at least 10% of patients on PYRUKYND® were headache, upper respiratory tract infection, initial insomnia, diarrhea and fatigue. Serious TEAEs were reported in 11.0% and 15.3% of patients on PYRUKYND® and placebo, respectively; 2.3% and 1.2%, respectively, were considered treatment-related. During the 48-week double-blind period, 5.8% of the patients in the PYRUKYND® arm experienced a TEAE leading to discontinuation compared to 1.2% of patients in the placebo arm. The TEAEs leading to

discontinuation of PYRUKYND®, each of which occurred in one patient, were diarrhea, paresthesia oral, concurrent anxiety and insomnia, initial insomnia, supraventricular tachycardia, fatigue, hypertransaminasemia, hepatitis C, hepatic cancer, and renal mass. The TEAE that led to discontinuation of the one patient on placebo was blood creatine phosphokinase increase.

As indicated above, during the double-blind periods of ENERGIZE and ENERGIZE-T, two patients on PYRUKYND® experienced events of hepatocellular injury. In addition, during the open-label extension periods of both trials, a total of three patients experienced events of hepatocellular injury after switching from placebo to PYRUKYND®. All of these events occurred within the first six months of exposure to PYRUKYND® and liver tests improved following discontinuation of PYRUKYND®.

Based on the results of the ENERGIZE and ENERGIZE-T trials, in December 2024 we announced that we filed regulatory applications for PYRUKYND® for the treatment of adult patients with non-transfusion-dependent and transfusion-dependent alpha- or beta-thalassemia with the FDA, EMA and Kingdom of Saudi Arabia and United Arab Emirates health authorities and we included in our regulatory applications hepatocellular injury as an important potential risk of PYRUKYND® in patients with thalassemia and proposed monthly monitoring of liver tests for the first six months of treatment with PYRUKYND®. We updated our PYRUKYND® clinical trial protocols across all indications to incorporate monthly monitoring of liver tests for the first six months of treatment and updated the U.S. Prescribing Information, or USPI, for PYRUKYND® for the treatment of hemolytic anemia in adults with PK deficiency to reflect the aforementioned risk of hepatocellular injury and recommended monitoring.

- RISE UP, a phase 2/3 study evaluating the efficacy and safety of PYRUKYND® in SCD patients who are 16 years of age or older, have had between two and 10 sickle cell pain crises, or SCPCs, in the past 12 months, and have hemoglobin within the range of 5.5 to 10.5 g/dL during screening. We enrolled 79 patients in the phase 2 portion of the trial, with 26 patients in the 50 mg twice daily mitapivat arm, 26 patients in the 100 mg twice daily mitapivat arm and 27 patients in the placebo arm. The primary endpoints of the phase 2 portion of the trial were hemoglobin response, defined as ≥ 1 g/dL increase in average hemoglobin concentration from week 10 to week 12 compared to baseline, and safety. In June 2023, we announced the phase 2 portion of this trial had achieved its primary endpoint of hemoglobin response in patients in both the 50 mg and 100 mg twice daily mitapivat arms. 46.2% of patients (n=12) in the 50 mg twice daily mitapivat arm and 50.0% of patients (n=13) in the 100 mg twice daily mitapivat arm achieved a hemoglobin response, compared to 3.7% of patients (n=1) in the placebo arm (2-sided p=0.0003 and 0.0001, respectively). In December 2023, we announced the following additional results of the phase 2 portion of the trial: (i) the least-squares mean (95% confidence interval) for average change from baseline in hemoglobin levels, from week 10 through week 12, for patients in the 50 mg twice daily mitapivat, 100 mg twice daily mitapivat, and placebo arms, respectively, was 1.11 (0.77, 1.45) g/dL, 1.13 (0.79, 1.47) g/dL, and 0.05 (−0.28, 0.39) g/dL; (ii) we observed improvements in annualized rates of SCPCs as the annualized rate of SCPCs (95% confidence interval) for patients in the 50 mg twice daily and 100 mg twice daily mitapivat arms, respectively, was 0.83 (0.34, 1.99) and 0.51 (0.16, 1.59), compared to 1.71 (0.95, 3.08) for patients in the placebo arm; (iii) we observed improvement in patient-reported fatigue scores in the 50 mg twice daily mitapivat arm compared to the placebo arm, and the least-squares mean (95% confidence interval) for average changes from baseline in patient-reported fatigue score, from week 10 through week 12, for patients in the 50 mg twice daily mitapivat, 100 mg twice daily mitapivat, and placebo arms, respectively, was −3.80 (−7.16, −0.45), −0.10 (−3.27, 3.08), and −0.17 (−3.40, 3.07). The safety profile for mitapivat observed in the phase 2 portion of the trial was generally consistent with previously reported data in other studies of SCD and other hemolytic anemias. The most common TEAEs in the 50 mg BID, 100 mg BID, and placebo arms, respectively, were: headache (n=6, 6, 7), arthralgia (n=3, 5, 9), dysmenorrhea (n=0, 3, 0), pain (n=3, 3, 2), pain in extremity (n=1, 3, 6), back pain (n=4, 2, 3), nausea (n=1, 2, 4), fatigue (n=4, 1, 5), and influenza-like illness (n=1, 1, 3). There were no serious TEAEs attributed to mitapivat and there were no AEs leading to drug reduction, discontinuation, interruption or death in either the mitapivat or the placebo arms. Of the 79 patients enrolled in the study, 73 continued into the Phase 2 open-label extension period. In October 2023, we enrolled the first patient in the phase 3 portion of this trial and we have since enrolled over 200 patients worldwide. The phase 3 portion includes a 52-week randomized, placebo-controlled period in which participants will be randomized in a 2:1 ratio to receive the recommended (100 mg twice daily) PYRUKYND® dose level or the placebo. The primary endpoints are hemoglobin response, defined as ≥1 g/dL increase in average hemoglobin from week 24 through week 52 compared to baseline, and annualized rate of SCPCs. The secondary endpoints include additional clinical efficacy measures related to anemia, hemolysis, erythropoiesis, patient-reported fatigue and pain, annualized frequency of hospitalizations for SCPCs, and change from baseline in six minute walk test. Participants who complete either the phase 2 or phase 3 portion will have the option to move into a 216-week open-label extension period to continue to receive PYRUKYND®. We have completed enrollment and expect to announce topline data for this trial in late 2025, with a potential U.S. commercial launch in 2026, if approved.

- Extension studies evaluating the long-term safety, tolerability and efficacy of treatment with PYRUKYND® in pediatric patients from ACTIVATE-kids and ACTIVATE-kidsT, our completed double-blind phase 3 studies evaluating the efficacy and safety of PYRUKYND® as a potential treatment for PK deficiency in not regularly transfused and regularly transfused patients between one and 18 years old, respectively.

  We announced topline data for ACTIVATE-kidsT in August 2024. A total of 49 patients were enrolled in ACTIVATE-kidsT, with 32 randomized to mitapivat twice-daily and 17 randomized to matched placebo. 30 patients (93.8%) in the mitapivat arm and 16 (94.1%) in the placebo arm completed the 32-week double-blind period of the study. The primary endpoint of ACTIVATE-kidsT is transfusion reduction response, defined as ≥33% reduction in total RBC transfusion volume from week 9 through week 32 of the double-blind period. Using Bayesian methodology, the prespecified statistical criterion for the primary endpoint in ACTIVATE-kidsT was not met using low or moderate borrowing of data from the ACTIVATE-T study in adults. In the study, 28.1% of patients in the mitapivat arm achieved the primary endpoint of transfusion reduction response, compared to 11.8% of patients in the placebo arm. Transfusion-free response and normal hemoglobin response were secondary endpoints in this study and only observed in patients in the mitapivat arm. In the 32-week double-blind treatment period, mitapivat was generally safe and well-tolerated, with safety results consistent with the safety profile for mitapivat previously observed in adults with PK deficiency who are regularly transfused.

  We announced topline data for ACTIVATE-kids in February 2025. A total of 30 patients were enrolled in ACTIVATE-kids, with 19 randomized to mitapivat twice-daily and 11 randomized to matched placebo. All patients in both treatment arms completed the 20-week double-blind period of the study. The primary endpoint of ACTIVATE-kids is percentage of patients with hemoglobin response, defined as ≥1.5 g/dL increase in hemoglobin concentration from baseline that is sustained at two or more scheduled assessments at weeks 12, 16, and 20 during the double-blind period. Using Bayesian methodology, the prespecified statistical criterion for the primary endpoint in ACTIVATE-kids was met using a range of relative borrowing from the adult ACTIVATE study, for all possible borrowing weights (ranging from 0 to 1). In addition, the pre-specified supportive analysis based on traditional methodology comparing the hemoglobin response rate for mitapivat versus placebo provided further evidence that the primary endpoint was met. There were 31.6% of patients in the mitapivat arm achieving a hemoglobin response compared to 0% of patients in the placebo arm; the 95% confidence interval for the difference in hemoglobin response rates between mitapivat and placebo was >0 (95% CI=10.8% to 52.7%). In addition, improvements in changes from baseline for markers of hemolysis (indirect bilirubin, lactate dehydrogenase and haptoglobin) were observed in the mitapivat arm compared to the placebo arm. In the 20-week double-blind period of the study, a similar proportion of patients had AEs in the mitapivat and placebo arms and there were no discontinuations of study treatment due to AEs or for any reason. The safety results from the trial were consistent with the safety profile for mitapivat previously observed for adult patients with PK deficiency who are not regularly transfused.
- An extension study evaluating the long-term safety, tolerability and efficacy of treatment with PYRUKYND® in patients from ACTIVATE and ACTIVATE-T, our completed pivotal trials of PYRUKYND® in not regularly transfused and regularly transfused adult patients with PK deficiency.
- An extension study evaluating the long-term safety, tolerability and efficacy of treatment with PYRUKYND® in patients from DRIVE PK, our completed global phase 2, first-in-patient, open-label safety and efficacy clinical trial of PYRUKYND® in adult, not regularly transfused patients with PK deficiency.

Tebapivat: Novel PK Activator

We are developing tebapivat, a novel PK activator for the potential treatment of LR MDS and SCD. Tebapivat has been granted orphan drug designation for the treatment of MDS by the FDA.

We have completed a phase 1 clinical trial evaluating tebapivat in healthy volunteers and patients with SCD, and initiated a phase 2 clinical trial of tebapivat in adult patients with SCD in the second quarter of 2025.

We also initiated a phase 2a clinical trial of tebapivat in adults with LR MDS in the third quarter of 2022, and the trial has completed enrollment with 22 patients, including 12 patients classified as non-transfused and 10 patients classified as low transfusion burden. Patients received 5 mg of tebapivat once daily for up to 16 weeks. The two primary endpoints of the trial were transfusion independence (for patients classified as low transfusion burden), defined as transfusion-free for ≥ eight consecutive weeks during the 16-week treatment period, and hemoglobin response, defined as a ≥ 1.5 g/dL increase from baseline in the average hemoglobin concentration measured from week 8 through week 16.

In November 2023, we announced that we achieved clinical proof-of-concept in the phase 2a portion of the trial. We observed that four of the 10 patients with low transfusion burden achieved the transfusion independence endpoint, and one of the 22 patients achieved the hemoglobin response endpoint in the 16-week treatment period. The safety profile observed was consistent with data reported in the healthy volunteer study of tebapivat. 19 patients elected to enroll in the extension period for

up to 156 weeks. We evaluated the phase 2a trial results and assessed the impact of those results on the phase 2b portion of the protocol, and based on the data generated in the phase 2a portion of the trial, we increased the dosage levels evaluated in the phase 2b portion of the trial, which we initiated in the third quarter of 2024. We expect to complete enrollment in this phase 2b trial in late 2025.

Other Programs

In addition to the aforementioned development programs, we are developing AG-181, a PAH stabilizer for the potential treatment of PKU, for which we filed an IND in December 2023. We initiated a phase 1 clinical trial of AG-181 in healthy volunteers in the first quarter of 2024, and initiated the multiple ascending dose portion of the trial in the second quarter of 2025. Also, in July 2023, we entered into a license agreement with Alnylam for the development and commercialization of products containing or comprised of an siRNA preclinical development candidate discovered by Alnylam and targeting the TMPRSS6 gene, and we are developing a product candidate, AG-236, for the potential treatment of patients with PV. We filed an IND with the FDA for AG-236 for the treatment of PV which cleared in June 2025.

We initiated a phase 1 clinical trial evaluating AG-236 in healthy volunteers in July 2025.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, business development, commercial, legal, information technology and human resources functions. Other significant costs include facility-related costs not otherwise included in research and development expenses, legal fees relating to patent and corporate matters, and fees for accounting and consulting services.

We anticipate that our selling, general and administrative expenses will increase in the future to support continued research and development activities, and ongoing and future commercialization activities related to our portfolio, including the ongoing commercialization of PYRUKYND® and any of our other product candidates, which may include the hiring of additional personnel.

Critical Accounting Estimates

Our critical accounting estimates are those which require the most significant judgments and estimates in the preparation of our condensed consolidated financial statements. We have determined that our most critical accounting estimates are those relating to revenue recognition, accrued research and development expenses and stock-based compensation. As of June 30, 2025, there have been no material changes to our existing critical accounting estimates discussed in Part II, Item 7 of our Annual Report on Form 10-K for the year ended December 31, 2024.

Results of Operations

Comparison of the three and six months ended June 30, 2025 and 2024

Revenues

(In thousands)	Three Months Ended June 30, 2025	Three Months Ended June 30, 2024	Six Months Ended June 30, 2025	Six Months Ended June 30, 2024
Revenues:				
Product revenue, net	$ 12,455	$ 8,615	$ 21,181	$ 16,804
Total revenue	$ 12,455	$ 8,615	$ 21,181	$ 16,804

Total Revenue - Three Months Ended June 30, 2025 vs. Three Months Ended June 30, 2024 – The increase in total revenue of $3.8 million for the three months ended June 30, 2025 compared to the three months ended June 30, 2024 was due to increased volume associated with PYRUKYND®.

Total Revenue - Six Months Ended June 30, 2025 vs. Six Months Ended June 30, 2024 – The increase in total revenue of $4.4 million for the six months ended June 30, 2025 compared to the six months ended June 30, 2024 was due to increased volume associated with PYRUKYND®.

Total Operating Expenses

(In thousands)	Three Months Ended June 30, 2025	Three Months Ended June 30, 2024	Six Months Ended June 30, 2025	Six Months Ended June 30, 2024
Operating expenses:				
Cost of sales	$ 1,702	$ 1,495	$ 2,787	$ 2,122
Research and development	91,940	77,401	164,683	146,021
Selling, general and administrative	45,869	35,536	87,396	66,550
Total operating expenses	$ 139,511	$ 114,432	$ 254,866	$ 214,693

Total Operating Expenses - Three Months Ended June 30, 2025 vs. Three Months Ended June 30, 2024 – The increase in total operating expenses of $25.1 million for the three months ended June 30, 2025 compared to the three months ended June 30, 2024 was primarily due to an increase in research and development expenses of $14.5 million, which is described below under Research and Development Expenses, and an increase in selling, general and administrative expenses of $10.3 million, driven by an increase in commercial-related activities as we prepare for the potential approval of PYRUKYND® in thalassemia.

Total Operating Expenses - Six Months Ended June 30, 2025 vs. Six Months Ended June 30, 2024 – The increase in total operating expenses of $40.2 million for the six months ended June 30, 2025 compared to the six months ended June 30, 2024 was primarily due to an increase in selling, general and administrative expenses of $20.8 million, driven by an increase in commercial-related activities as we prepare for the potential approval of PYRUKYND® in thalassemia, and an increase in research and development expenses of $18.7 million which is described below under Research and Development Expenses.

Research and Development Expenses

Our research and development expenses, by major program, are outlined in the table below:

(In thousands)	Three Months Ended June 30, 2025	Three Months Ended June 30, 2024	Six Months Ended June 30, 2025	Six Months Ended June 30, 2024
PK activator (PYRUKYND®)	$ 29,809	$ 27,968	$ 51,130	$ 54,004
Novel PK activator (tebapivat)	7,852	4,488	13,240	6,383
In-process research and development	10,000	—	10,000	—
Other research and platform programs	5,394	7,270	8,838	10,955
Total direct research and development expenses	53,055	39,726	83,208	71,342
Compensation and related expenses	27,594	27,476	60,584	55,110
Facilities and IT related expenses & other	11,291	10,199	20,891	19,569
Total indirect research and development expenses	38,885	37,675	81,475	74,679
Total research and development expense	$ 91,940	$ 77,401	$ 164,683	$ 146,021

Total Research and Development Expenses - Three Months Ended June 30, 2025 vs. Three Months Ended June 30, 2024 – The increase in total research and development expenses of $14.5 million for the three months ended June 30, 2025 compared to the three months ended June 30, 2024 was primarily due to a $13.3 million increase in our direct expenses. The increase in direct expenses was primarily due to in-process research and development as a result of the $10.0 million milestone payment associated with the agreement with Alnylam discussed above under Overview.

Total Research and Development Expenses - Six Months Ended June 30, 2025 vs. Six Months Ended June 30, 2024 – The increase in total research and development expenses of $18.7 million for the six months ended June 30, 2025 compared to the six months ended June 30, 2024 was due to a $11.9 million increase in our direct expenses and a $6.8 million increase in our indirect expenses. The increase in direct expenses was primarily due to in-process research and development as a result of the $10.0 million milestone payment associated with the agreement with Alnylam discussed above under Overview, and an increase in tebapivat costs due to increased costs associated with clinical trials of tebapivat in patients with SCD and LR MDS. These increases were partially offset by a decrease in PYRUKYND® costs due to lower process development expenses, lower costs associated with the phase 3 ACTIVATE-Kids and ACTIVATE-KidsT trials, and lower costs associated with the phase 3 ENERGIZE and ENERGIZE-T trials, partially offset by increased professional expenses. The increase in our indirect expenses was primarily due to an increase in compensation and related expenses, driven principally by workforce-related expenses.

Other Income and Expense

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2025	2024	2025	2024
Interest income, net	$ 14,513	$ 8,120	$ 30,600	$ 17,009
Other income, net	523	1,579	1,776	3,213

Other Income and Expense - Three Months Ended June 30, 2025 vs. Three Months Ended June 30, 2024 – The increase in interest income, net in the three months ended June 30, 2025 compared to the three months ended June 30, 2024 was primarily attributable to increased return on our investments and an increased investment balance.

Other Income and Expense - Six Months Ended June 30, 2025 vs. Six Months Ended June 30, 2024 – The increase in interest income, net in the six months ended June 30, 2025 compared to the six months ended June 30, 2024 was primarily attributable to increased return on our investments and an increased investment balance.

Net Loss

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2025	2024	2025	2024
Net loss	$ (112,020)	$ (96,118)	$ (201,309)	$ (177,667)

Net Loss - Three Months Ended June 30, 2025 vs. Three Months Ended June 30, 2024 – The increase in net loss for the three months ended June 30, 2025 compared to the three months ended June 30, 2024 was primarily driven by the increase in research and development expenses discussed above in *Research and Development Expenses*, and the increase in selling, general and administrative expenses discussed above in *Total Operating Expenses,* partially offset by the increase in interest income, net discussed above in *Other Income and Expense*, and the increase in product revenue discussed above in *Revenue*.

Net Loss - Six Months Ended June 30, 2025 vs. Six Months Ended June 30, 2024 – The increase in net loss for the six months ended June 30, 2025 compared to the six months ended June 30, 2024 was primarily driven by the increase in selling, general and administrative expenses discussed above in *Total Operating Expenses* and the increase in research and development expenses discussed above in *Research and Development Expenses*, partially offset by the increase in interest income, net discussed above in *Other Income and Expense,* and the increase in product revenue discussed above in *Revenue*.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, and through March 31, 2021, we financed our operations primarily through proceeds from the sale of our royalty rights, commercial sales of TIBSOVO®, funding received from our collaboration agreements, private placements of our preferred stock, our initial public offering of our common stock and concurrent private placement of common stock to an affiliate of Celgene, and our follow-on public offerings. Following the sale of our oncology business to Servier on March 31, 2021, we have financed and expect to continue to finance our operations primarily through cash on hand, potential royalty payments with respect to the Retained Earn-Out Rights, the actual and potential future sales of PYRUKYND® and, potentially,

collaborations, strategic alliances, licensing arrangements and other nondilutive strategic transactions. In addition, we may pursue opportunistic debt offerings, and equity or equity-linked offerings.

On March 31, 2021, we completed the sale of our oncology business to Servier. The transaction included the sale of our oncology business, including TIBSOVO®, our clinical-stage product candidates vorasidenib, AG-270 and AG-636, and our oncology research programs, for a payment of approximately $1.8 billion in cash at the closing, subject to certain adjustments, and the right to the Vorasidenib Milestone Payment, as well as a royalty of 5% of U.S. net sales of TIBSOVO® from the close of the transaction through loss of exclusivity, and the Vorasidenib Royalty Rights. The Vorasidenib Milestone Payment, Vorasidenib Royalty Rights and royalty payments related to TIBSOVO® are referred to as contingent payments and recognized as income when realizable. Servier also acquired our co-commercialization rights for Bristol Myers Squibb's IDHIFA® and the right to receive a $25.0 million potential milestone payment under our prior collaboration agreement with Celgene, and following the sale Servier has agreed to conduct certain clinical development activities within the IDHIFA® development program. As discussed in Note 1, *Overview and Basis of Presentation*, in October 2022, we sold our rights to the royalty on U.S. net sales of TIBSOVO® to Sagard for $131.8 million, but we retained our rights to the Vorasidenib Milestone Payment and Vorasidenib Royalty Rights.

In August 2024, the FDA approved vorasidenib for adult and pediatric patients 12 years and older with Grade 2 astrocytoma or oligodendroglioma with a susceptible IDH1 or IDH2 mutation, following surgery including biopsy, sub-total resection, or gross total resection. In September 2024, we received the Vorasidenib Milestone Payment from Servier and recognized income of $200.0 million within the milestone payment from gain on sale of oncology business line item in our consolidated statements of operations for the three months ended September 30, 2024. In May 2024, we entered into a purchase and sale agreement to sell the Vorasidenib Royalty Rights to Royalty Pharma Investments 2019 ICAV, or Royalty Pharma, for $905.0 million in cash, or the Upfront Payment. The sale was contingent upon FDA approval of vorasidenib and other customary closing conditions.

Upon consummation of the sale in August 2024, Royalty Pharma acquired 100% of the Vorasidenib Royalty Rights payments made by Servier on account of up to $1.0 billion in U.S. net sales for each calendar year. In addition, any such Vorasidenib Royalty Rights payments made by Servier on account of U.S. net sales in each calendar year in excess of $1.0 billion will be split, with Royalty Pharma having the rights to a 12% earn-out on those excess payments and Agios retaining the rights to a 3% earn-out on those excess payments, or the Retained Earn-Out Rights. As a result of the sale, we recognized income of $889.1 million ($905.0 million net of fees of $15.9 million) within the gain on sale of contingent payments line item in our consolidated statements of operations for the three months ended September 30, 2024. Royalty income related to the Retained Earn-Out Rights, if any, will be recognized in the period when realizable.

Our cash, cash equivalents and marketable securities balance was $1.3 billion at June 30, 2025. The Retained Earn-Out Rights discussed above are our only committed potential external sources of funds. We cannot predict what success, if any, Servier may have in the United States with respect to the sale of vorasidenib, and consequently, we cannot estimate the amount of payments, if any, we may receive on account of the Retained Earn-Out Rights.

Cash Flows

The following table provides information regarding our cash flows for the six months ended June 30, 2025 and 2024:

	Six Months Ended June 30,	
(In thousands)	**2025**	**2024**
Net cash used in operating activities	$ (188,613)	$ (172,456)
Net cash provided by investing activities	191,553	161,806
Net cash provided by financing activities	1,684	6,963
Net change in cash and cash equivalents	$ 4,624	$ (3,687)

Net cash used in operating activities. Cash used in operating activities of $188.6 million during the six months ended June 30, 2025 was primarily due to operating expenses driven by research and development costs described above under *Research and Development Expenses*, partially offset by cash received from interest income of $31.5 million and product revenues of $22.0 million.

Cash used in operating activities of $172.5 million during the six months ended June 30, 2024 was primarily due to operating expenses driven by research and development costs described above under *Research and Development Expenses*, partially offset by cash received from interest income of $19.3 million and product revenues of $17.6 million.

Net cash provided by investing activities. Cash provided by investing activities of $191.6 million during the six months ended June 30, 2025 was primarily due to higher proceeds from maturities and sales of marketable securities than purchases of marketable securities.

Cash provided by investing activities of $161.8 million during the six months ended June 30, 2024 was primarily due to higher proceeds from maturities and sales of marketable securities than purchases of marketable securities.

Net cash provided by financing activities. Cash provided by financing activities of $1.7 million during the six months ended June 30, 2025, was due to net proceeds received from stock option exercises and purchases made pursuant to our 2013 Employee Stock Purchase Plan, or 2013 ESPP.

Cash provided by financing activities of $7.0 million during the six months ended June 30, 2024 was due to net proceeds received from stock option exercises and purchases made pursuant to our 2013 ESPP.

Funding Requirements

We expect our expenses to increase as we continue the research, development and clinical trials of, seek marketing approvals for, and commercialize our product candidates in our portfolio, including as we continue to commercialize PYRUKYND®. If we obtain additional marketing approvals for PYRUKYND® in thalassemia or in other indications, or outside of the United States or for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution.

We expect that our existing cash, cash equivalents and marketable securities as of June 30, 2025, together with anticipated product revenue and interest income, will provide the financial independence to prepare for potential PYRUKYND® commercial launches in thalassemia and SCD, advance our existing programs, and opportunistically expand our pipeline through both internally and externally discovered assets. Our expectations regarding our long-term funding requirements are based on assumptions that may prove to be wrong, and we may need additional capital resources to fund our operating plans and capital expenditure requirements.

Our future capital requirements will depend on many factors, including:

- the amount and timing of future revenue received from commercial sales of PYRUKYND® or any of our product candidates for which we may receive marketing approval;
- the amount of payments, if any, we may receive on account of the Retained Earn-Out Rights;
- the costs and timing of our ongoing and future commercialization activities, including product manufacturing, sales, marketing and distribution for PYRUKYND® in the approved jurisdictions and indications and for any product candidate for which we may receive approval;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our product candidates;
- the costs associated with in-licensing or acquiring assets for pipeline growth, including the amount and timing of future milestone and royalty payments potentially payable to Alnylam pursuant to the license agreement;
- the costs, timing and outcome of regulatory review of our product candidates, including with respect to regulatory submissions for PYRUKYND® for the treatment of thalassemia;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- our ability to successfully execute on our strategic plans;
- operational delays due to public health epidemics; and
- operational delays, disruptions and/or increased costs associated with global economic and political developments, rising global energy prices or energy shortages or rationing.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs primarily through cash on hand, potential royalty payments with respect to the Retained Earn-Out Rights, the actual and potential future sales of PYRUKYND® and, potentially, collaborations, strategic alliances, licensing arrangements and other nondilutive strategic transactions. In addition, we may pursue opportunistic debt offerings, and equity or equity-linked offerings. We do not have any committed external source of funds other than the Retained Earn-Out Rights. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, selling or licensing our assets, making capital expenditures or declaring dividends.

If we raise funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings

when needed or on attractive terms, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations

During the six months ended June 30, 2025, there were no material changes to our contractual obligations and commitments described under Management's Discussion and Analysis of Financial Condition and Results of Operations in our Annual Report on Form 10-K for the year ended December 31, 2024.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risk related to changes in interest rates. As of June 30, 2025 and December 31, 2024, we had cash, cash equivalents and marketable securities of $1.3 billion and $1.5 billion, respectively, consisting primarily of investments in U.S. Treasuries, government securities, corporate debt securities and certificates of deposit. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are primarily in short-term marketable securities. Our marketable securities are subject to interest rate risk and could fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, we do not believe an immediate and uniform 100 basis point change in interest rates would have a material effect on the fair market value of our investment portfolio.

We are also exposed to market risk related to changes in foreign currency exchange rates. We have contracts with CROs and contract manufacturing organizations that are located in Asia and Europe and are denominated in foreign currencies. We are subject to fluctuations in foreign currency rates in connection with these agreements. We do not currently hedge our foreign currency exchange rate risk. As of June 30, 2025 and December 31, 2024, we had minimal or no liabilities denominated in foreign currencies.

Item 4. Controls and Procedures

Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, evaluated, as of the end of the period covered by this Quarterly Report on Form 10-Q, the effectiveness of our disclosure controls and procedures. Based on that evaluation of our disclosure controls and procedures as of June 30, 2025, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures as of such date are effective at the reasonable assurance level. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports it files or submits under the Exchange Act is accumulated and communicated to its management, including its principal executive officer and principal financial officer, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act, that occurred during the fiscal quarter ended June 30, 2025 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

Item 1A. Risk Factors

The following risk factors and other information included in this Quarterly Report on Form 10-Q should be carefully considered. The risks and uncertainties described below are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 16 of this Quarterly Report on Form 10-Q for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to the Discovery, Development, and Commercialization of our Products and Product Candidates

If we do not successfully commercialize PYRUKYND® and other products for which we receive approval, our prospects may be substantially harmed.

PYRUKYND® (mitapivat) is approved for use by the FDA for the treatment of hemolytic anemia in adults with PK deficiency in the United States and by the European Commission for the treatment of PK deficiency in adult patients in the EU. Additionally, we received marketing authorization in Great Britain for PYRUKYND® for the treatment of PK deficiency in adult patients under the European Commission Decision Reliance Procedure. In December 2024, we announced that we submitted an sNDA, to the FDA for PYRUKYND® for the treatment of adult patients with non-transfusion dependent and transfusion-dependent alpha- or beta-thalassemia, which was accepted with standard review and granted a PDUFA goal date of September 7, 2025. Also in December 2024, we announced that we submitted an MAA to the EMA, and regulatory applications to the Kingdom of Saudi Arabia and United Arab Emirates health authorities for PYRUKYND® for the treatment of adult patients with non-transfusion dependent and transfusion-dependent alpha- or beta-thalassemia.

Our ability to generate meaningful revenue from PYRUKYND® will depend heavily on our successful development and commercialization of the product. We generated $21.2 million and $16.8 million of net product revenues from sales of PYRUKYND® in the six months ended June 30, 2025 and 2024, respectively. In connection with our regulatory approval in the EU and Great Britain, we are currently providing access to PYRUKYND® on a for charge and free of charge basis for eligible patients in those jurisdictions through a global managed access program. We provide access to PYRUKYND® for adult patients with PK deficiency in other jurisdictions upon request through the global managed access program, on either a free of charge or for charge basis. Beyond the global managed access program, we have entered into the NewBridge Agreement and the Avanzanite Agreement for commercialization of PYRUKYND® in certain regions outside of the United States and we continue to evaluate other options for the commercialization of PYRUKYND® outside of the United States, including through exploring potential partnership opportunities.

The development and commercialization of PYRUKYND® could be unsuccessful if:

- the medical community and third-party payors do not accept PYRUKYND® as safe, efficacious and cost-effective in the approved jurisdictions and indications;
- we fail to maintain the necessary financial resources and expertise to manufacture, market and sell PYRUKYND®;
- we fail to develop, implement and maintain effective marketing, sales and distribution strategies and operations for the development and commercialization of PYRUKYND®, including under the NewBridge Agreement and the Avanzanite Agreement;
- we fail to continue to develop, validate and maintain a commercially viable manufacturing process for PYRUKYND® that is compliant with current good manufacturing practices, or cGMP;
- we fail to successfully obtain third party reimbursement and generate and sustain commercial demand that results in expected sales of PYRUKYND®;
- PYRUKYND® becomes subject to unfavorable pricing regulations and third-party reimbursement practices;
- we encounter any third-party patent interference, derivation, inter partes review, post-grant review, reexamination or patent infringement claims with respect to PYRUKYND®;
- we fail to comply with regulatory and legal requirements applicable to the sale of PYRUKYND®;
- competing drug products are approved for the same indications as PYRUKYND®;
- significant safety, manufacturing and/or quality risks are identified;
- PYRUKYND® fails to gain and/or maintain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community;
- a significant number of eligible patients with PK deficiency are not prescribed PYRUKYND® and, if they are, such patients do not stay on treatment; or

- PYRUKYND® does not demonstrate acceptable safety and efficacy in current or future clinical trials, or otherwise does not meet applicable regulatory standards for approval in other indications.

If we experience significant delays or an inability to successfully develop and commercialize PYRUKYND®, our business would be materially harmed.

We depend heavily on the success of our clinical-stage product candidates, including the potential approval of PYRUKYND® for the treatment of thalassemia or SCD in the United States and in other jurisdictions. Clinical trials of our product candidates may not be successful for a number of important reasons. If we or our collaborators are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the identification of our product candidates and the development of our most advanced clinical programs, including PYRUKYND® and tebapivat. Our ability to generate meaningful product revenue will depend heavily on the successful clinical development and eventual commercialization of our current and any future product candidates, including PYRUKYND®. We cannot be certain that we will obtain marketing approval of PYRUKYND® in jurisdictions with pending or potential future marketing applications for thalassemia, nor can we be certain that we will obtain marketing approval of PYRUKYND® for any other indication or in other jurisdictions.

We, and any collaborators, are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities, such as the EMA, impose similar requirements in foreign jurisdictions. Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The clinical development of our product candidates is susceptible to the risk of failure inherent at any stage of product development. Moreover, we, or any collaborators, may experience any of a number of possible unforeseen adverse events in connection with clinical trials, many of which are beyond our control, including:

- we, or our collaborators, may fail to demonstrate efficacy in a clinical trial or across a broad population of patients;
- it is possible that even if one or more of our product candidates has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. For example, many compounds that initially showed promise in earlier stage testing for treating specific indications have later been found to cause side effects that prevented further development of the compound;
- our product candidates may have undesirable side effects or other unexpected characteristics or otherwise expose participants to unacceptable health risks, causing us, our collaborators or our investigators, regulators or institutional review boards or the data safety monitoring board for such trial to halt, delay, interrupt, suspend or terminate the trials or cause us, or any collaborators, to abandon or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective;
- if our product candidates have undesirable side effects, it could result in a more restrictive label or the addition of safety warnings, or it could result in the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. For example, in January 2025, the USPI for PYRUKYND® for the treatment of hemolytic anemia in adults with PK deficiency was updated to include information regarding hepatocellular injury observed in clinical trials in patients with thalassemia treated with PYRUKYND® at a higher dose than recommended for patients with PK deficiency;
- clinical trials of our product candidates may produce negative or inconclusive results, and we, or our collaborators, may decide, or regulators may require us, to conduct additional clinical trials, including testing in more subjects, or abandon product development programs;
- regulators or institutional review boards may not authorize us, our collaborators or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we or our collaborators may have delays in reaching or failing to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;

- the number of patients required for clinical trials of our product candidates may be larger than we anticipate; enrollment in these clinical trials, which may be particularly challenging for some of the orphan diseases we target in our rare disease programs, may be slower than we anticipate; or participants may drop out of these clinical trials at a higher rate than we anticipate;
- third-party contractors used by us or our collaborators may fail to comply with regulatory requirements or meet their contractual obligations in a timely manner, or at all;
- significant preclinical study or clinical trial delays could shorten any periods during which we, or any collaborators, may have the exclusive right to commercialize our product candidates or allow our competitors, or the competitors of any collaborators, to bring products to market before we, or any collaborators, do;
- the cost of clinical trials of our product candidates may be greater than anticipated; and
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate.

In December 2016, we withdrew our IND for AG-519, our second PK activator, following verbal notification of a clinical hold from the FDA relating to a previously disclosed case of drug-induced cholestatic hepatitis which occurred in our phase 1 clinical trial of AG-519 in healthy volunteers. Although these decisions and this hepatic adverse event finding do not affect our ongoing clinical trials for PYRUKYND® or tebapivat, we cannot provide any assurances that there will not be other treatment-related severe adverse events in our other clinical trials, or that our other trials will not be placed on clinical hold in the future.

Our failure to successfully complete clinical trials of our product candidates and obtain regulatory approval to market any of our product candidates could significantly harm our business.

We may engage in in-licensing transactions or acquisitions that could disrupt our business, cause dilution to our stockholders or reduce our financial resources.

We may engage in transactions to in-license products, technologies or assets or to acquire other products, technologies, assets or businesses. As part of the evolution of our research organization, we plan to prioritize in-licensing or acquiring assets for future pipeline growth. For example, in July 2023, we entered into a license agreement with Alnylam for the development and commercialization of products containing or comprised of an siRNA development candidate discovered by Alnylam and targeting the TMPRSS6 gene, and we are developing a product candidate, AG-236, for the potential treatment of patients with PV.

Our ability to successfully in-license or acquire assets and develop product candidates following such transactions is unproven. If we do identify additional suitable candidates or assets for in-licensing transactions or acquisitions, we may not be able to make such transactions on favorable terms, or at all. Such transactions may require us to relinquish rights to develop product candidates in certain indications, limit our ability to pursue certain targets or require us to make significant milestone or royalty payments to third parties upon achievement of certain events. For example, we are responsible to pay up to $130.0 million in potential development and regulatory milestones, in addition to sales milestones as well as tiered royalties on annual net sales, if any, of any licensed products, under the license agreement with Alnylam. Further, any in-licensing transaction or acquisitions we undertake may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or an in-licensing transaction or issue our common stock or other equity securities to the stockholders of the counterparty, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business, product or technology that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and non-disruptive manner. Such transactions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot ensure that following any transaction we would achieve the expected synergies to justify the transactions. We cannot predict the number, timing or size of future transactions or the effect that any such transactions might have on our operating results.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We or our collaborators may not be able to initiate, continue or complete clinical trials for our product candidates if we or they are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or analogous regulatory authorities outside the United States.

Patient enrollment is affected by factors including:

- prevalence and severity of the disease under investigation;
- availability and efficacy of approved medications for the disease under investigation;
- eligibility criteria for the study in question;
- perceived risks and benefits of the product candidate under study;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients; and
- the impact of any health epidemics, pandemics or other contagious outbreaks or geopolitical events, such as war.

We generally focus our development activities on genetically or biomarker defined patients most likely to respond to our therapies. As a result, the potential patient populations for our clinical trials are narrowed, and we may experience difficulties in identifying and enrolling a sufficient number of patients in our clinical trials.

In addition, some of our competitors may have ongoing or planned clinical trials for product candidates that would treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. Competition for eligible patients may make it particularly difficult for us to enroll a sufficient number of patients to complete our clinical trials for our product candidates in a timely and cost-effective manner.

In addition, we have a small number of clinical trial sites for certain clinical trials in the Middle East that could be affected by the current armed conflict in the region.

We rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and while we have agreements governing their committed activities, we have limited influence over their actual performance. Our or our collaborators' inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether, or result in increased development costs for our product candidates, which could have an adverse effect on our business, results of operations and financial condition.

Results of preclinical studies and early clinical trials may not be predictive of results of later-stage clinical trials.

The outcome of our preclinical studies and early clinical trials may not be predictive of the success of our later clinical trials, and positive results of our completed clinical trials do not necessarily predict success in our future clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier stages of development, and we could face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we or our collaborators believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. If we fail to receive positive results in clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced product candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

Interim and preliminary data from clinical trials that we announce or publish from time to time may change as more patient data becomes available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may announce or publish interim or preliminary data from our clinical trials. Interim or preliminary data from clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. We also make assumptions, estimations, calculations, and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully evaluate all data. Preliminary or interim data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we have previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could be material and could significantly harm our reputation and business prospects.

We conduct clinical trials at sites outside the United States. The FDA may not accept data from trials conducted in such locations, and the conduct of trials outside the United States could subject us to additional delays and expense.

We conduct and plan to conduct one or more clinical trials with one or more trial sites that are located outside the United States. The acceptance by the FDA or other regulatory authorities of study data from clinical trials conducted outside their jurisdiction may be subject to certain conditions or may not be accepted at all.

Where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and may result in current or future product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

Conducting clinical trials outside the United States also exposes us to additional risks, including risks associated with foreign exchange fluctuations, compliance with foreign manufacturing, customs, shipment and storage requirements, cultural differences in medical practice and clinical research, diminished protection of intellectual property in some countries, and interruptions or delays in our trials resulting from geopolitical events, such as war or terrorism.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. We are prioritizing investment in advancing our late lead-optimization research, while continuing to progress our registration-enabling clinical programs. Our resource allocation decisions may cause us to fail to capitalize on viable commercial medicines or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable medicines. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We or others may later discover that PYRUKYND®, or any of our product candidates that may receive marketing approval in the future, is less effective than previously believed or causes undesirable side effects that were not previously identified, which could compromise our ability, or that of any collaborators, to market the product.

It is possible that our clinical trials, or those of any collaborators, may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, including PYRUKYND®, we, or others, discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;

- we, or any collaborators, may be required to recall the product, change the way the product is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular product;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of warnings on the product label;
- we, or any collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or any collaborators, could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

For example, in January 2025, the USPI for PYRUKYND® for the treatment of hemolytic anemia in adults with PK deficiency was updated to include information regarding liver injury observed in patients with thalassemia treated with PYRUKYND® at a higher dose than recommended for patients with PK deficiency.

PYRUKYND®, or any of our product candidates that may receive marketing approval in the future, may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

PYRUKYND®, or any of our product candidates that may receive marketing approval in the future, may fail to gain and/or maintain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community, which could limit our ability to generate product revenue and impact our ability to become profitable. The degree of market acceptance of PYRUKYND® and any of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- the prevalence and severity of any side effects;
- the ability to offer our medicines for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- ensuring uninterrupted product supply;
- the strength of sales, marketing and distribution support, including under any distribution agreement with third parties;
- sufficient third-party coverage or reimbursement; and
- product labeling or product insert requirements of the FDA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling.

If we are unable to maintain sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we may not be successful in commercializing PYRUKYND® or any of our product candidates if they are approved.

We have limited experience in the sale, marketing and distribution of pharmaceutical products. To achieve commercial success for approved medicines for which we retain sales and marketing responsibilities, we must either continue to develop our sales and marketing organization or outsource these functions to other third parties. We have established sales and marketing capabilities to support our commercialization of PYRUKYND® for the treatment of hemolytic anemia in adults with PK deficiency in the United States and have expanded these capabilities to support the potential commercial launch of PYRUKYND® in thalassemia in the United States.

We may need to further build our sales and marketing infrastructure, either directly or with third-party partners to commercialize PYRUKYND® in additional markets outside of the United States, or to commercialize any of our other product candidates for which we obtain marketing approval. For example, we have entered into distribution agreements with third parties for the commercialization of PYRUKYND® in certain jurisdictions outside of the United States, including the NewBridge Agreement and the Avanzanite Agreement.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive, time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our medicines on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future medicines;
- the lack of complementary medicines to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or the profitability of product revenue to us are likely to be lower than if we were to market and sell any medicines that we develop ourselves. In addition, we may not be successful in entering into such arrangements with third parties or we may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our medicines effectively. If we do not establish or maintain sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing PYRUKYND® or any of our product candidates for which we obtain marketing approval.

We provide certain development estimates related to the development and regulatory approval of PYRUKYND® and our product candidates. If we do not achieve our projected development or regulatory approval estimates in the timeframes we announce and expect, the commercialization of our products may be delayed and, as a result, our stock price may decline.

From time to time, we provide estimates related to the development of PYRUKYND® and our product candidates. We also estimate the timing of the anticipated accomplishment of various scientific, preclinical, clinical, regulatory and other product development goals. These estimates may include the commencement or completion of clinical trials, the timing of completing enrollment, the timing for reporting clinical trial results and the timing of submission of regulatory filings in various jurisdictions. From time to time, we may publicly announce our estimates, including the timing of certain milestones related to our product candidates. All of these estimates are and will be based on numerous assumptions. The actual results and timing of our preclinical studies, clinical trials and regulatory submissions can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If our estimates change or we do not meet the timing of our estimates as publicly announced, or at all, the commercialization of our products may be delayed or never achieved and, as a result, our stock price may decline.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

We face competition with respect to PYRUKYND® and tebapivat and our other product candidates, and we will face competition with respect to any product candidates that we may seek to develop or commercialize in the future. Potential competitors may include major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the indications for which we are developing our product or our product candidates, such as PK deficiency, thalassemia, SCD, LR MDS, PKU, and PV. For example, Merck and Bristol-Myers Squibb Company, or BMS, are marketing a therapy to treat beta thalassemia and LR MDS, and are conducting clinical trials for alpha thalassemia and LR MDS patients that are erythropoeisis-stimulating agent naïve and non-transfusion dependent; Geron Corporation recently announced FDA approval of a treatment for adults with LR MDS with transfusion-dependent anemia; Takeda Pharmaceutical Company Limited, or Takeda with Keros Therapeutics, Inc. are developing a therapy to treat LR-MDS; Novartis International AG is marketing a therapy and has another molecule in clinical trials to treat SCD; Emmaus Life Sciences is marketing a therapy to treat SCD; BioMarin Pharmaceutical Inc. is marketing and conducting clinical trials for therapies to treat PKU; Pfizer Inc. is conducting clinical trials for therapies in SCD; Novo Nordisk A/S is conducting clinical trials for the treatment of alpha and beta thalassemia and SCD; Sanofi is conducting clinical trials for a therapy in SCD; bluebird is marketing a gene therapy to treat transfusion-dependent beta-thalassemia and SCD; Vertex, with CRISPR, is

marketing a gene therapy targeting SCD and transfusion-dependent beta-thalassemia; Fulcrum Therapeutics Inc. is conducting clinical trials for a potential treatment for SCD; BMS is conducting clinical trials for a potential treatment for SCD; PTC Therapeutics, Inc. and Otsuka Pharmaceutical Co., Ltd are conducting clinical trials for potential treatments for PKU; PharmaEssentia Corp and Incyte Corporation are marketing therapies to treat PV, and Protagonist Therapeutics with Takeda, Ionis Pharmaceuticals, Inc. with Ono Pharmaceutical Co., Ltd, Italfarmaco S.p.A., Disc Medicine, Inc., Merck & Co., Inc., and Silence Therapeutics are developing therapies to treat PV; Rocket Pharma LTD is developing a therapy for the treatment of PK deficiency; and a number of other biotechnology companies have product candidates in clinical development in similar indications as ours.

There are a variety of treatment options available, including a number of marketed enzyme replacement therapies, or ERTs, for treating patients with rare diseases. In addition to currently marketed therapies, there are also a number of products that are either ERTs, gene therapies or PK activators in various stages of clinical development to treat rare diseases. These products in development may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies or for which there are no approved treatments. As a result, they may provide significant competition for any of our product candidates for which we obtain marketing approval.

Our competitors may develop products that are more effective, safer, more convenient or less costly than PYRUKYND® or any product candidates that we are developing or that would render PYRUKYND® or our product candidates obsolete or non-competitive. In addition, our competitors may discover biomarkers that more efficiently measure metabolic pathways than our methods, which may give them a competitive advantage in developing potential products. Our competitors may also obtain marketing approval from the FDA or other regulatory authorities for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and globally marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and clinical stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring or in-licensing technologies complementary to, or necessary for, our programs.

If the FDA does not grant our products, if and when approved, appropriate periods of regulatory exclusivity before approving generic or follow-on versions of our products, the sales of our products could be adversely affected.

With FDA approval of an NDA, the product covered by the application is specified as a “reference-listed drug” in the FDA’s publication, “Approved Drug Products with Therapeutic Equivalence Evaluations,” or the Orange Book. Manufacturers may seek approval of generic versions of reference-listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States.

In support of an ANDA, a generic manufacturer need not conduct clinical trials. Rather, the sponsor generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference-listed drug and that the generic version is bioequivalent to the reference-listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any reference-listed drug may be lost to the generic product.

A manufacturer may also submit an NDA under section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or FDCA, that references the FDA’s prior approval of the innovator product or preclinical studies and/or clinical trials that were not conducted by, or for, the sponsor and for which the sponsor has not obtained a right of reference. A 505(b)(2) NDA product, or follow-on-product, may be for a new or improved version of the original reference listed drug.

The FDA may not approve an ANDA or 505(b)(2) NDA until any applicable period of regulatory exclusivity for the reference-listed drug has expired, subject to certain exceptions.

In the event that a generic or follow-on manufacturer is somehow able to obtain FDA approval without adherence to the periods of regulatory exclusivity, the competition that our approved products may face from generic and follow-on versions could negatively impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on our investments in those product candidates.

In addition, if there are patents listed for our drug products in the Orange Book, ANDAs and 505(b)(2) NDAs would be required to include a certification as to each listed patent indicating whether the sponsor intends to challenge the patent. We cannot predict which, if any, patents in our current portfolio or patents we may obtain in the future will be eligible for listing in the Orange Book, how any generic or follow-on competitor would address such patents, whether we would sue on any such patents or the outcome of any such suit.

Product liability lawsuits against us or any collaborators could cause us or our collaborators to incur substantial liabilities and could limit commercialization of any medicines that we or they may develop.

We and any collaborators face a risk of product liability exposure related to our product candidates in human clinical trials and face an even greater risk as we or they commercially sell any medicines, including PYRUKYND®. If we or any collaborators cannot successfully defend ourselves or themselves against claims that our product candidates or medicines caused injuries, we or they could incur substantial costs and liabilities. Regardless of merit or eventual outcome, liability claims may also result in, among other things, decreased demand for any product candidates or medicines that we may develop, reputational harm and lost revenue.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur.

Our internal information technology systems, or those of any third parties with which we contract, may fail or suffer security breaches, loss of data or other disruptions which could result in a material disruption of our product development programs, compromise sensitive information related to our business or prevent us from accessing critical information, trigger legal obligations, potentially exposing us to liability, competitive or reputational harm or otherwise adversely affecting our business and financial results.

Despite the implementation of security measures, our internal information technology systems and those of third parties with which we contract are vulnerable to damage from computer viruses, worms and other destructive or disruptive software, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors or business partners, or from cyber incidents by malicious third parties. Cybersecurity incidents are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cybersecurity incidents could include the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cybersecurity incidents also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient. Attackers may use artificial intelligence and machine learning to launch more automated, targeted and coordinated attacks against targets. We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company, including personal information of our employees. We may not be able to anticipate all types of security threats, and we may not be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched, and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations or hostile foreign governments or agencies.

System failures, accidents, cybersecurity incidents or security breaches could cause interruptions in our operations, and could result in a material disruption of our clinical and commercialization activities and business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from completed or future trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and our product research, development and commercialization efforts could be delayed. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events.

If a material breach of our security or that of our vendors occurs, the market perception of the effectiveness of our security measures could be harmed, and, as a result, we could lose business and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. Although we develop and maintain processes, systems and controls designed to prevent these events from occurring, and we have a process to assess, identify and manage threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be

eliminated entirely. We cannot guarantee that the measures we have taken to date, and actions we may take in the future, will be sufficient to prevent any cyber-attacks or security breaches.

We are subject to stringent privacy laws, information security laws, regulations, policies and contractual obligations related to data privacy and security and changes in such laws, regulations, policies, contractual obligations and failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally-identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information, including comprehensive regulatory systems in the United States and the EU. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and we must devote significant resources and funds to understanding and complying with this changing landscape. Our efforts to comply with the evolving data protection rules may be unsuccessful. It is possible that these laws may be interpreted, enforced and applied in a manner that is inconsistent with our practices.

There are numerous U.S. federal and state laws and regulations related to the privacy and security of personal information. In particular, regulations promulgated pursuant to the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information.

The FTC has been particularly focused on the unpermitted processing of health and genetic data through its recent enforcement actions and is expanding the types of privacy violations that it interprets to be "unfair" under Section 5 of the FTC Act of 1914, as well as the types of activities it views to trigger the Health Breach Notification Rule. The FTC is also in the process of developing rules related to commercial surveillance and data security that may impact our business.

A number of states have passed comprehensive privacy laws and other states are strongly considering or in the process of enacting such laws. These laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data (which includes health data in some cases). In addition, Congress has also been debating passing a federal privacy law, and there are also states that are specifically regulating health information. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

There are also significant privacy and data security laws that apply in Europe and other countries. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in the European Economic Area, or EEA, and the processing of personal data that takes place in the EEA, is regulated by the GDPR. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and policies. While many other countries outside of the EEA loosely follow GDPR as a model, other laws contain different or conflicting provisions.

Failure to comply with any of these laws and regulations could result in litigation, regulatory investigations or enforcement actions against us, orders to changes our practices, systems or policies, breaches of our contracts, fines, imprisonment of company officials and public censure, civil or criminal penalties, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects. Even if we are not determined to have violated these laws, litigation or government investigations into these issues typically require the expenditure of significant resources and generate negative publicity.

Risks Related to Our Financial Position

We face challenges as a less diversified company.

The success of the rare disease business is subject to various risks and uncertainties, including the possibility that we may not be able to successfully commercialize PYRUKYND®, the possibility that PYRUKYND® is not approved for thalassemia, the possibility that PYRUKYND® is not approved for SCD, the possibility of adverse clinical and other developments in respect of PYRUKYND®, tebapivat or our other product candidates, and unanticipated changes in applicable laws and regulations that may adversely affect the rare disease business.

We may be more susceptible to changing market conditions, including fluctuations and risks particular to the markets for patients with rare diseases, than a more diversified company, which could adversely affect our business, financial condition and

results of operations. In addition, even with the FDA approval of PYRUKYND® for PK deficiency, the diversification of our revenues, costs and cash flows has diminished following the sale of our oncology business. Our results of operations, cash flows, working capital and financing requirements may be subject to increased volatility and our ability to fund capital expenditures and investments or satisfy other financial commitments may be diminished.

Raising additional capital may restrict our operations, require us to relinquish rights to our technologies or product candidates or cause dilution to our stockholders.

Until such time, if ever, as we can generate substantial product revenue, including from sales of PYRUKYND®, we expect to finance our cash needs primarily through cash on hand, potential royalty payments with respect to annual U.S. net sales of vorasidenib in excess of $1.0 billion, or the Retained Earn-Out Rights, and, potentially, collaborations, strategic alliances, licensing arrangements and other nondilutive strategic transactions. In addition, we may pursue opportunistic debt offerings, and equity or equity-linked offerings. We do not have any committed external source of funds other than the potential Retained Earn-Out Rights described above and we cannot be certain we will ever receive any payments as a result of the Retained Earn-Out Rights. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may require us to enter into agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, selling or licensing our assets, making capital expenditures or declaring dividends. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

If we raise funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

If our existing capital is insufficient to fund our operating expenses and capital expenditures, we will need to raise capital, and if we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect to incur significant expenses as we continue to advance our ongoing activities. Our estimate as to what extent we expect our existing cash, cash equivalents, and marketable securities to be available to fund our operating expenses and capital expenditures is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds. If we are unable to raise additional funds when needed or on attractive terms, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Our future capital requirements will depend on many factors, including:

- the amount and timing of future revenue received from commercial sales of PYRUKYND® and any of our other product candidates for which we may receive marketing approval;
- the amount of payments, if any, we may receive on account of the Retained Earn-Out Rights;
- the costs and timing of our ongoing and future commercialization activities, including product manufacturing, sales, marketing and distribution, for PYRUKYND® in the approved jurisdictions and indications and for any product candidate for which we may receive approval;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our product candidates;
- the costs associated with in-licensing or acquiring assets for pipeline growth, including the amount and timing of future milestone and royalty payments payable to Alnylam pursuant to the license agreement;
- the costs, timing and outcome of regulatory review of our product candidates, including with respect to regulatory submissions for PYRUKYND® for the treatment of thalassemia;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- our ability to successfully execute on our strategic plans; and

- operational delays, disruptions and/or increased costs associated with public health pandemics, global economic and political developments, rising global energy prices or energy shortages or rationing.

We have historically incurred operating losses. We expect to incur losses in the future and may never achieve or maintain profitability.

We have a history of incurring operating losses. Our net losses for the six months ended June 30, 2025 and 2024 were $201.3 million million and $177.7 million million, respectively. As of June 30, 2025, we had an accumulated deficit of $350.2 million. Following receipt of marketing approval in February 2022, we are commercializing PYRUKYND® for the treatment of hemolytic anemia in adults with PK deficiency in the United States.

We are currently providing access to PYRUKYND® on either a free of charge or for charge basis for eligible patients in the EU and Great Britain through a global managed access program, and we provide access to PYRUKYND® for adult patients with PK deficiency in other jurisdictions through the global managed access program on either a free of charge or for charge basis. Beyond the global managed access program, we have entered into the NewBridge Agreement and the Avanzanite Agreement for commercialization of PYRUKYND® in certain regsions outside of the United States and we continue to evaluate other options for the commercialization of PYRUKYND® outside of the United States, including through exploring potential partnership opportunities.

We expect to finance our operations primarily through cash on hand, potential royalty payments with respect to the Retained Earn-Out Rights, and, potentially, collaborations, strategic alliances, licensing arrangements and other nondilutive strategic transactions. In addition, we may pursue opportunistic debt offerings, and equity or equity-linked offerings. We expect to continue to incur significant expenses and net losses until such time as we are able to report profitable results. The net losses we incur may fluctuate significantly from quarter to quarter and year to year. We anticipate that we will incur significant expenses if and as we:

- prepare for and commercially launch PYRUKYND® for approved indications in approved jurisdictions;
- continue to establish and maintain a sales, marketing and distribution infrastructure to commercialize PYRUKYND® and other product candidates for which we may obtain marketing approval;
- initiate and continue clinical trials for our products and product candidates;
- continue our research and preclinical development of our product candidates and seek to identify additional product candidates;
- seek marketing approvals for our product candidates that successfully complete clinical trials;
- require the manufacture of larger quantities of product candidates for clinical development and commercialization;
- maintain, expand and protect our intellectual property portfolio;
- add additional personnel to support our product research and development and planned future commercialization efforts and our operations; and
- acquire or in-license other product candidates, medicines and technologies.

To become and remain profitable, we must develop and successfully commercialize medicines with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those medicines for which we may obtain marketing approval and satisfying any post-marketing requirements. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

Income, sales, use or other tax laws, statutes, rules, or regulations could be enacted or amended at any time, which could affect our business or financial condition, including causing potentially adverse impacts to our effective tax rate, tax liabilities, and cash tax obligations. For example, the Inflation Reduction Act, or IRA, was signed into law in August 2022, and the One Big Beautiful Bill Act, or OBBBA, was signed into law in July 2025. The OBBBA contains numerous tax provisions that we are currently in the process of evaluating, and which may affect our business or financial condition. Regulatory guidance under the IRA, the OBBBA, and other tax-related legislation is and continues to be forthcoming, and such guidance could ultimately

increase or lessen the impact of these laws on our business and financial condition. In addition, it is uncertain if and to what extent various states will conform to changes to federal tax legislation.

Risks Related to Our Dependence on Third Parties

We rely and expect to continue to rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.

We do not independently conduct clinical trials of any of our product candidates. We rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. In addition, we currently rely and expect to continue to rely on third parties to conduct some aspects of our research and preclinical testing. Any of these third parties may terminate their engagements with us, some in the event of an uncured material breach and some at any time. If any of our relationships with these third parties terminate, we may not be able to enter into similar arrangements with alternative third-parties or to do so on commercially reasonable terms. Switching or adding additional third parties involves additional cost and requires management time and focus. As a result, delays may occur in our product development activities. Although we seek to carefully manage our relationships with our CROs, we could encounter such challenges or delays that could have a material adverse impact on our business, financial condition and prospects.

Our reliance on third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our responsibility to comply with any such standards. We and these third parties are required to comply with current good clinical practices, or cGCP, which are regulations and guidelines enforced by the FDA, the competent authorities of the member states of the EEA and comparable foreign regulatory authorities for all of our product candidates in clinical development. We cannot be certain that a given regulatory authority will determine that any of our clinical trials comply with cGCP regulations. Regulatory authorities enforce these cGCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA, or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We are exposed to risk of fraud or other misconduct by such third parties.

Furthermore, third parties on whom we rely may also have relationships with other entities, some of which may be our competitors. In addition, these third parties are not our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical, nonclinical, and preclinical programs.

If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, or if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised, our clinical trials may be extended, delayed or terminated and we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to successfully commercialize our medicines.

If either we or any third parties on which we rely are adversely impacted by geopolitical events, rising global energy costs or energy shortages or rationing, delays may occur in our product development activities, which delays could have a material adverse impact on our business, financial condition and prospects.

Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our medicines, producing additional losses and depriving us of potential product revenue.

We contract with third parties for the manufacture of our product candidates for preclinical and clinical testing and for commercialization.

We do not have any manufacturing or supply chain-related facilities. We currently rely, and expect to continue to rely, on third-party manufacturers for the materials and manufacture of our product candidates for preclinical and clinical testing and for commercial supply of PYRUKYND® and any product candidate for which we obtain marketing approval.

Although we have entered into long-term supply agreements for commercial supply of PYRUKYND® with third-party manufacturers, we may be unable to establish similar long-term supply agreements with third-party manufacturers with respect to our other product candidates or to do so on acceptable terms. Even if we are able to establish such agreements, reliance on third-party manufacturers entails additional risks, including: reliance on the third party for regulatory compliance, quality

assurance, environmental and safety and pharmacovigilance reporting; the possible breach of the manufacturing agreement by the third party; and the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with cGMPs, regulations or similar regulatory requirements on a global basis. Our failure, or the failure of our third-party manufacturers, to comply with currently applicable regulations, or regulations or specifications to which we become subject in the future, could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or medicines, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business and results of operations.

In addition, we currently rely on foreign third-party manufacturers and/or CROs, including those in China, and will likely continue to rely on foreign third-party manufacturers and/or CROs in the future. Foreign third-party manufacturers and/or CROs may be subject to U.S. legislation, including sanctions, trade restrictions and other foreign regulatory requirements which could increase the cost or reduce the supply of material or services available to us, delay the procurement or supply of such material or services, or have an adverse effect on our ability to secure significant commitments from governments to purchase our potential therapies. Moreover, in September 2024, the U.S. House of Representatives passed the BIOSECURE Act, and the Senate advanced a substantially similar bill, but it did not pass. If these bills become law, or similar laws are passed, they would have the potential to severely restrict the ability of companies like ours to contract with certain Chinese biotechnology companies of concern without losing the ability to contract with, or otherwise received funding from, the U.S. government, and it is possible that some of our contractual counterparties could be impacted. Such disruptions could have adverse effects on the development of our product candidates and our business operations.

If either we or any third parties on which we rely are adversely impacted by restrictions resulting from the emergence of public health epidemics, by rising global energy costs or energy shortages or rationing and/or geopolitical events, our supply chain may be disrupted, limiting our ability to manufacture our product candidates for our clinical trials and research and development operations and our product for commercialization.

Any performance failure on the part of our existing or future manufacturers could delay preclinical development, clinical development, marketing approval or our commercialization efforts. Due to the volatility of the supply networks globally, we have obtained regulatory approval for redundant supply of raw materials for PYRUKYND®, and have an ongoing program to monitor supply, including establishing safety stocks. While we maintain a broad safety stock of drug substance and drug product, we do not currently have arrangements in place for redundant supply of drug substance and drug product. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer. Although we believe that there are several potential alternative manufacturers who could manufacture our product or our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or medicines may adversely affect our future profit margins and our ability to commercialize any medicines that receive marketing approval on a timely and competitive basis.

We may depend on collaborations with third parties for the development and commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We may seek collaborations for the development and commercialization of our product candidates with large and mid-size pharmaceutical companies and biotechnology companies or with other third parties. We face significant competition in seeking appropriate collaborators. Collaborations are complex and time-consuming to negotiate and document. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. Collaborators may have rights that restrict us from entering into future agreements on certain terms with potential collaborators.

If we enter into any such arrangements with collaborators, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities. Collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing, which may result in a need

for additional capital to pursue further development or commercialization of the applicable product candidate. Collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation. Disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our medicines or product candidates or that result in costly litigation or arbitration that diverts management attention and resources. In addition, our ability to enter into arrangements with collaborators in specific regions, such as the Middle East, may be affected by localized geopolitical unrest or military conflict, such as the current armed conflict in the region.

In addition, we do not have direct experience commercializing products outside of the United States and such efforts may depend on our ability to find a suitable collaborator. For example, we have entered into the NewBridge Agreement and the Avanzanite Agreement for the commercialization of PYRUKYND® in certain jurisdictions outside of the United States.

Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent or trade secret protection for our medicines and technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize medicines and technology similar or identical to ours, and our ability to successfully commercialize our medicines and technology may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary medicines and technology. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and medicines that are important to our business. We do not yet have issued patents for all our most advanced product candidates in all markets in which we intend to commercialize but we continue to actively pursue patent protection for our assets around the world.

The patent prosecution process is costly and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify and/or file patent applications on every aspect of our research and development output that is or may be eligible for patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who may have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. There is also the possibility that loss or theft of data or records may jeopardize the ability to seek patent protection or impede the progress or drafting of patent applications.

We have licensed patent rights, and in the future may license additional patent rights, from third parties. Such licenses may be accompanied by milestone and/or royalty payment obligations. These licensed patent rights may be valuable to our business, and we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology or medicines underlying such licenses. We cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. If any such licensors fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected. In addition to the foregoing, the risks associated with patent rights that we license from third parties also apply to patent rights we own.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our technology or medicines or that effectively prevent others from commercializing competitive technologies and medicines. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

The United States maintains a first inventor to file system in which, assuming the other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent. We may be subject to a third-party pre-issuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, revocation, reexamination, post-grant and inter partes review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize medicines without infringing third-party patent rights.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us or otherwise provide us with any competitive advantage. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of the patent or in one or more patent claims being narrowed or invalidated, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and medicines. Given the significant amount of time required for the discovery, development, preclinical and clinical testing and regulatory review and approval of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. In such circumstances we would be relying primarily on regulatory or marketing exclusivity to exclude others from commercializing a generic version of our products.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents and other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive, time consuming and have uncertain outcomes. For example we may file patent infringement suits against any company that files and ANDA containing a Paragraph IV patent certification for mitapivat. In addition, a court may decide that a patent of ours is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Third parties may initiate legal proceedings alleging that we or our collaborators are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product and product candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. We have in the past, are and may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our medicines and technology, including opposition, derivation, revocation, reexamination, post-grant and inter partes review or interference proceedings before the USPTO or other patent offices around the world. For example, two of the European patents in our mitapivat portfolio, neither being the primary compound patent, have been challenged in opposition proceedings in the European Patent Office. The revocation of either of these European patents could potentially allow additional competitor drugs, if approved, to enter the European marketplace earlier than anticipated.

Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we or one of our collaborators are found to infringe a third party's intellectual property rights, we or they could be required to obtain a license from such third party to continue developing and marketing our medicines and technology. However, we or our collaborators may not be able to obtain any required license on commercially reasonable terms or at all. Even if we or our collaborators were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us. We or our collaborators could be forced, including by court order, to cease developing and commercializing the infringing technology or medicine. In addition, we or our collaborators could be found liable for monetary damages. A finding of infringement could prevent us or our collaborators from commercializing our product and product candidates or force us to cease some of our business operations, which could materially harm our business. Claims

that we or our collaborators have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

Many of our employees, consultants or advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to our organization.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

If we are unable to protect the confidentiality of our confidential information related to our proprietary platforms and technology, our business and competitive position could be harmed.

In addition to seeking patents for some of our technology and medicines, we also rely on maintaining the confidentiality of unpatented know-how, technology and other proprietary information, to maintain our competitive position. For example, we consider the confidential information and know-how related to our cellular metabolism technology platform to be our primary intellectual property assets in this space. Unpatented proprietary technical information and know-how can be difficult to protect.

We seek to protect this proprietary technical information and know-how, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information (including through use of generative artificial intelligence technologies), and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated proprietary information is difficult, expensive and time-consuming, and the outcome is unpredictable. If any of our proprietary technical information and know-how were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. Moreover, we anticipate that with respect to this platform, at least some of this technical information and know-how will, over time, be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel skilled in the art from academic to industry scientific positions.

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

The marketing approval process is expensive, time-consuming and uncertain, and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we or our collaborators are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we or they will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, record keeping, labeling, storage, approval, advertising, promotion, sale and distribution, export and import, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and comparable regulatory authorities in other countries.

Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we or our collaborators ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved medicine not commercially viable.

The FDA, EMA and other foreign regulatory authorities have substantial discretion in the approval process. Accordingly, it is possible that the FDA or EMA may refuse to accept for substantive review any NDA, supplemental NDA or MAA that we submit for our product candidates, or may conclude after review of our data that our marketing application is insufficient to obtain marketing approval of our product candidates. The applicable regulator may require that we conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data before reconsidering our applications. Depending on the extent of these or any other FDA- or EMA-required trials or studies, approval of any marketing applications that we submit may be delayed by several years, or may require us to expend more resources than we planned. It is also possible that additional trials or studies, if performed and completed, may not be considered sufficient by the FDA or EMA to approve any marketing applications. We may not be successful in obtaining FDA or EMA approval of our product candidates on a timely basis, or ever. We have limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party CROs to assist us in this process.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or a comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

Further, the process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application.

In addition, recent and potential future courts decisions and administrative law cases may result in additional legal challenges to regulations and guidance issued by federal regulatory agencies, including the FDA and CMS, that we have relied on and intend to rely on in the future. Any such challenges, if successful, could have a material impact on our business. In addition to potential changes to regulations and agency guidance as a result of legal challenges, these decisions may result in increased regulatory uncertainty and delays in and other impacts to the agency rulemaking process, any of which could adversely impact our business and operations.

Additionally, our ability to develop and market new drug products may be impacted based on current or future litigation in the federal court system challenging the FDA's approval of other companies' drugs. Depending on the outcome of this type of

litigation, our ability to develop new drug product candidates and to maintain approval of existing drug products could be at risk and our efforts to develop and market new drug products could be delayed, undermined or subject to protracted litigation.

If we or our collaborators experience delays in obtaining approval or if we or they fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenue will be materially impaired.

Failure to obtain marketing approval in foreign jurisdictions would prevent our medicines from being marketed in such jurisdictions and any of our medicines that are approved for marketing in such jurisdiction will be subject to risk associated with foreign operations.

In December 2024, we announced that we submitted an MAA to the EMA, and regulatory applications to the Kingdom of Saudi Arabia and United Arab Emirates health authorities for PYRUKYND® for the treatment of adult patients with non-transfusion dependent and transfusion-dependent alpha- or beta-thalassemia. In order to market and sell our medicines in the EU and many other foreign jurisdictions, we or our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many foreign countries, a product must be approved for reimbursement before the product can be approved for sale in that country. We or our collaborators may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Moreover, approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. Although we have received marketing authorization for PYRUKYND® for the treatment of adults with PK deficiency in the EU and Great Britain, we may not be able to file for additional marketing approvals and may not receive necessary approvals to commercialize our medicines in any other foreign market.

In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, EU pharmaceutical legislation is currently undergoing a complete review process. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may be substantially revised before adoption, which is not anticipated before early 2026. The revisions may have a significant impact on the EU pharmaceutical industry and our business in the long term.

We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including tariffs and trade barriers; economic weakness, including inflation, or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue; and workforce uncertainty in countries where labor unrest is more common than in the United States. In addition, we do not have direct experience commercializing products outside of the United States and such efforts may depend on our ability to find a suitable collaborator. For example, we have entered into the NewBridge Agreement and the Avanzanite Agreement for the commercialization of PYRUKYND® in certain jurisdictions outside of the United States.

Fast track designation and/or priority review designation by the FDA or PRIME designation in the EU may not actually lead to a faster development or regulatory review or approval process, nor does it ensure approval of the product candidate.

We may in the future seek fast track designation or priority review designation for our product candidates.The FDA has broad discretion on whether to grant fast track designation and/or priority review designation to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Even if our product candidates receive fast track designation and/or priority review designation, we may not experience a faster development process, review or approval, if at all, compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

In addition, we may seek PRIME designation in the EU for our product candidates. The benefits of a PRIME designation include, among other things, the potential to qualify product for accelerated review. Even if our product candidates receive PRIME designation, we may not experience a faster development process, review or approval compared to conventional EMA procedures and it does not ensure or increase the likelihood of the EMA's grant of a marketing authorization.

We, or any collaborators, may not be able to obtain orphan drug designation or orphan drug exclusivity for our drug candidates and, even if we do, that exclusivity may not prevent the FDA or the EMA from approving competing drugs.

Regulatory authorities in some jurisdictions, including the United States and the EU, may designate drugs and biologics for relatively small patient populations as orphan drugs. Generally, if a product with an orphan drug designation subsequently

receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same product for that time period, except in certain limited circumstances. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. Moreover, even after an orphan drug is approved, the FDA can subsequently approve a different product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

We do not know if, when, or how the FDA or Congress may reevaluate or change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business or if we will be adversely impacted.

Any product or product candidate for which we or our collaborators obtain marketing approval could be subject to restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our medicines, when and if any of them are approved.

Any product or product candidate for which we or our collaborators obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such medicine, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and record keeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the medicine may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a REMS.

The FDA and other agencies, including the Department of Justice, or DOJ, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use and if we market our medicines for uses other than their respective approved indications, we may be subject to enforcement actions for off-label marketing. Violations of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws, which violations may result in the imposition of significant administrative, civil and criminal penalties.We will need to carefully navigate the FDA's regulations and this guidance to ensure compliance with the FDA's provisions governing promotion of our products.

Disruptions at the FDA and other government agencies from funding cuts, personnel losses, regulatory reform, government shutdowns and other developments could hinder our ability to obtain guidance from the FDA regarding our clinical development program and develop and secure approval of our product candidates in a timely manner, which would negatively impact our business.

If oversight and review activities by the FDA and comparable foreign regulatory authorities are disrupted, then our ability to develop and/or secure timely approval of our product candidates could be impacted in a negative manner. For example, the recent loss of FDA leadership and personnel could lead to disruptions and delays in FDA guidance, review and approval of our product candidates. In March 2025, the Secretary of HHS announced a reorganization and reduction in force, or RIF, across the HHS of approximately 20,000 employees, with FDA's workforce to decrease by 3,500 full-time employees. Thereafter, thousands of employees at the FDA were fired on April 1, 2025. Subsequently, there have been reports from the preliminary budget memorandum for HHS that the administration will propose an additional 30% cut in the overall budget for the Department, with a reduction of $700 million in funding at the FDA for the 2026 federal fiscal year.

Further, while the FDA's review of marketing applications and other activities for new drugs and biologics is largely funded through the user fee program established under PDUFA, it remains unclear how the administration's RIF and budget cuts will impact this program and the ability of the FDA to provide guidance and review our product candidates in a timely manner.

There is also substantial uncertainty as to how regulatory reform measures being implemented by the Trump administration across the government will impact the FDA and other federal agencies with jurisdiction over our activities. For example, President Trump has issued a number of executive orders that could have a significant impact on the manner in which the FDA conducts its operations and engages in regulatory and oversight activities. If these or other orders or executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Accordingly, if any of the foregoing developments and others impact the ability of the FDA to provide us with guidance or delay the FDA's review and processing of our regulatory submissions, our business would be negatively impacted.

Our relationships with healthcare providers, physicians and third-party payors are subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of PYRUKYND® and any product candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute PYRUKYND® and any other medicines for which we obtain marketing approval. Such laws and regulations include the federal Anti-Kickback Statue; the federal False Claims Act; HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act; the federal Physician Payments Sunshine Act; and analogous state and foreign laws and regulations.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of member states of the EU, or the EU Member States, such as the U.K. Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

PYRUKYND® or any product candidate that we commercialize may become subject to unfavorable pricing regulations and third-party reimbursement practices, which would harm our business.

We built our commercial infrastructure to support the commercialization of PYRUKYND® in adult PK deficiency in the United States, and have expanded this infrastructure to support the potential commercial launch of PYRUKYND® in thalassemia in the United States. The commercial success of PYRUKYND® or of any of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by third-party payors, including government health administration authorities and private health coverage insurers. If coverage and reimbursement is not available, or reimbursement is available only to limited levels, we, or any collaborators, may not be able to successfully commercialize PYRUKYND® or our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any future collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their investments.

In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors, and coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that requires us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Pricing and reimbursement for new drug products vary widely from country to country. Some

countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

As a result, we, or any collaborators, might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability or the ability of any collaborators to recoup our or their investment in one or more product candidates, even if our product candidates obtain marketing approval.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Third-party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability or that of any collaborators to sell PYRUKYND® or our product candidates profitably. These payors may not view our products as cost-effective, and coverage and reimbursement may not be available to our customers, or those of any collaborators, or may not be sufficient to allow our products to be marketed on a competitive basis. Cost-control initiatives could cause us, or any collaborators, to decrease the price we, or they, might establish for products, which could result in lower than anticipated product revenue. If the prices for our products decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. We cannot be sure that coverage will be available for PYRUKYND® or any product candidate that we, or any collaborator, may commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for PYRUKYND® or any of our product candidates for which we, or any collaborator, may obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Current and future healthcare reform legislation may increase the difficulty and cost for us and any collaborators to commercialize our drug candidates.

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any collaborators, to profitably sell PYRUKYND® or any other product candidate for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the price that we, or any collaborators, may receive for any approved products. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. This legislation resulted in aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which will remain in effect for six months into fiscal year 2032. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. President Trump recently revoked numerous executive orders issued by

President Biden, including at least two executive orders which where were designed to further implement the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The prices of prescription pharmaceuticals in the United States and foreign jurisdictions are subject to considerable legislative and executive actions and could impact the prices we obtain for our drug products, if and when approved, and/or the sustainability of those prices.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States.

We cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

On April 15, 2025, President Trump issued an executive order which directs HHS to take steps to reduce the prices of pharmaceutical products and repeats many of the proposals advanced during the first Trump administration, including directing the FDA to streamline and improve its existing drug importation program so as to make it easier for states to obtain approval without sacrificing the safety or quality of drug products. Other provisions of the executive order relate to the 340B program. With respect to the IRA's Medicare drug pricing program, the executive order, among other things, calls for alignment in "the treatment of small molecule prescription drugs with that of biological products, ending the distortion that undermines relative investment in small molecule prescription drugs, coupled with other reforms to prevent any increase in overall costs to Medicare and its beneficiaries."

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product or product candidates or additional pricing pressures.

In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In markets outside of the United States and the EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. In many countries, including those of the EU, the pricing of prescription pharmaceuticals is subject to governmental control and access. If pricing is set at unsatisfactory levels, our business could be materially harmed.

We are subject to U.S. and foreign export control, import, sanctions, anti-corruption and anti-money laundering laws with respect to our operations, and non-compliance with such laws can subject us to criminal and/or civil liability and harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Control, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. In addition, we may engage third party intermediaries to promote our clinical research activities abroad and/or to obtain necessary permits, licenses, and other regulatory approvals. We have entered into distribution agreements with third parties for the commercialization of PYRUKYND® in certain jurisdictions outside of the United States. We can be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners, and agents, even if we do not explicitly authorize or have actual knowledge of such activities.

Noncompliance with such laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or

injunctions, suspension and/or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage, and other collateral consequences. If any subpoenas, investigations, or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens.

Changes in and uncertainty surrounding U.S. trade policy could have a material adverse impact on our business, financial condition and results of operations.

The Trump administration recently initiated a series of tariff-related actions against U.S. trading partners. On April 2, 2025, the President issued an executive order announcing a "baseline" reciprocal tariff of 10% on all U.S. trading partners effective April 5, 2025, and higher individualized reciprocal tariffs on 57 countries (with certain product exemptions for pharmaceutical-related products, among others). Previously, the administration had imposed a 25% tariff on Canada and Mexico for goods not covered by the United States-Mexico-Canada Agreement, or USMCA, and tariffs equaling 20% on China. In response, several countries threatened retaliatory measures, including Canada and China, which then imposed retaliatory tariffs. Prior to when the country-specific reciprocal tariffs were scheduled to take effect, the administration delayed the effective date of such tariffs for all countries except China. Later, the U.S. and China reached a framework agreement that resulted in the suspension of the higher reciprocal tariffs on China until August 10, 2025. Three other countries, the United Kingdom, Vietnam and Indonesia, have also reached deals with the U.S. that include reduced tariff rates and other measures. The administration has not indicated the effective date for these deals. Recently, the administration announced an extension of the deadline for the effective date of the country-specific tariffs for all remaining countries until August 1, 2025.

Currently, the 10% baseline reciprocal tariff announced in April remains in effect, in addition to the other tariffs on China (a minimum of an additional 20% as of July 15, 2025) and Canada and Mexico (25% as of July 15, 2025 for goods that are not covered by the USMCA). Sustained uncertainty about, or the further escalation of, trade and political tensions between the United States and China could result in a disadvantageous research and manufacturing environment in China, particularly for U.S. based companies, including retaliatory restrictions that hinder or potentially inhibit our ability to rely on contract development and manufacturing organizations and other service providers that operate in China.

Separately, on April 16, 2025, the U.S. Department of Commerce announced an investigation under Section 232 of the Trade Expansion Act of 1962 into imports of pharmaceuticals and pharmaceutical ingredients, including finished drug products, medical countermeasures, critical inputs such as active pharmaceutical ingredients, and key starting materials, and derivative products of those items. The investigation will examine the impact of these imports on U.S. national security culminating in a decision by the President whether to take action to remedy any identified threats, including by imposing additional tariffs. The statute provides that the Commerce Department report must be completed within 270 days of initiation of the investigation and that the President must decide whether to act within 90 days of receiving the report.

As a result of changes in tariffs that have been announced and/or implemented, and the underlying uncertainty currently surrounding international trade, we could experience a negative impact to our costs of materials and production processes, and supply chain disruptions and delays as a result of any new tariff policies or trade restrictions. If we are unable to obtain necessary raw materials or product components in sufficient quantity and in a timely manner due to disruptions in the global supply chain caused by macroeconomic events and conditions, the development, testing and clinical trials of our product candidates may be delayed or infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business. We cannot yet predict the effect of the recently imposed U.S. tariffs on imports, or the extent to which other countries will impose quotas, duties, tariffs, taxes or other similar restrictions upon imports or exports in the future, nor can we predict future trade policy or the terms of any renegotiated trade agreements and their impact on our business.

The CREATES Act exposes us to possible litigation and damages by competitors who may claim that we are not providing sufficient quantities of our approved products on commercially reasonable, market-based terms for testing in support of their ANDAs and 505(b)(2) applications.

The Creating and Restoring Equal Access to Equivalent Samples Act of 2019, or the CREATES Act, authorizes sponsors of ANDAs and 505(b)(2) applications to file lawsuits against companies holding NDAs that decline to provide sufficient quantities of an approved reference drug on commercially reasonable, market-based terms, subject to certain exemptions.

If a sponsor were to bring an action under the statute and prevail in litigation, it is entitled to a court order directing the NDA holder to provide, without delay, sufficient quantities of the applicable product on commercially reasonable, market-based

terms, plus reasonable attorney fees and costs. Additionally, the statutory provisions authorize a federal court to award the sponsor an amount "sufficient to deter" the NDA holder from refusing to provide sufficient product quantities on commercially reasonable, market-based terms if the court finds, by a preponderance of the evidence, that the NDA holder did not have a legitimate business justification to delay providing the product or failed to comply with the court's order.

Although we intend to fully comply with the terms of these statutory provisions, we are still exposed to potential litigation and damages by competitors who may claim that we are not complying. Such litigation would subject us to additional costs, damages and reputational harm, which could lead to lower revenues. The CREATES Act may enable generic competition with PYRUKYND® and any of our product candidates, if approved, which could impact our ability to maximize product revenue.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our key executives and scientific leadership and to attract, retain and motivate qualified personnel.

We are highly dependent on the principal members of our management and scientific teams, each of whom is employed "at will," meaning we or they may terminate the employment relationship at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives. We cannot predict the likelihood, timing or effect of future transitions among our executive leadership.

Recruiting and retaining qualified scientific, clinical, manufacturing, regulatory and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies and universities and research institutions for similar personnel. Our consultants and advisors who assist us in formulating our research and development and commercialization strategy may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Furthermore, our flexible workplace policy which allows employees to work from home may make it difficult for us to maintain our corporate culture.

In the future we may experience growth in the number of our development, regulatory and sales and marketing personnel. To manage any anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations or regulations in other jurisdictions, provide accurate information to the FDA or other regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data accurately, disclose unauthorized activities to us, or comply with securities laws. Employee misconduct could also involve the improper use of information obtained in the course of

clinical trials or interactions with the FDA or other regulatory authorities, including for illegal insider trading activities, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Conduct and Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

Risks Related to Our Common Stock and Other Matters

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our Board of Directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our Board of Directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our Board of Directors;
- limit the manner in which stockholders can remove directors from our Board of Directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our Board of Directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our Board of Directors to issue preferred stock without stockholder approval, which could be used to institute a shareholder rights plan, or so-called “poison pill,” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our Board of Directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

The price of our common stock is volatile, which could result in substantial losses for purchasers of our common stock.

The trading price of our common stock has been, and may continue to be, volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. While the full extent of the economic impact of the recent increases in inflation rates (particularly as it relates to clinical- or manufacturing-related costs) may be difficult to assess or predict, such impacts have

already caused, and are likely to result in further, significant disruption of global financial markets, which may reduce our ability to access capital either at all or on favorable terms.

The market price for our common stock may be influenced by many factors, including:

- our success in launching and commercializing PYRUKYND®;
- announcements by us or our competitors of significant acquisitions, in-licensing arrangements, strategic partnerships, joint ventures, collaborations or capital commitments;
- the timing and results of clinical trials of product candidates, or our competitors' product candidates;
- regulatory actions with respect to our or our competitors' products or product candidates;
- commencement or termination of collaborations for our development programs;
- failure or discontinuation of any of our development programs;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our products, product candidates or development programs;
- the results of our efforts to develop additional product candidates and products;
- actual or anticipated changes in estimates as to financial results or development timelines;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or results of companies that are perceived to be similar to us;
- changes in estimates, evaluations or recommendations by securities analysts, that cover our stock or the failure by one or more securities analysts to continue to cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, political, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

In the past, following periods of volatility in the market price of a company's securities, securities class-action litigation often has been instituted against that company. Such litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert managements' attention and resources, which could seriously harm our business, financial condition, results of operations and prospects.

We also cannot guarantee that an active trading market for our shares will be sustained. An inactive trading market for our common stock may impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

Our financial condition and operating results also may fluctuate from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, our stockholders should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Our executive officers, directors and principal stockholders maintain the ability to significantly influence all matters submitted to stockholders for approval.

As of June 30, 2025, our executive officers, directors and principal stockholders, in the aggregate, beneficially owned shares representing a significant percentage of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons could significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

Under Section 382 and 383 of the Code and corresponding provisions of state law, if a company undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership by certain stockholders over a three-year period, the company's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change taxable income may be limited. Our prior equity offerings and other changes in our stock ownership, some of which are outside of our control, may have resulted or could in the future result in an ownership change. We completed a review of our changes in ownership through December 31, 2024, and determined that we did not have a qualified ownership change since our last review as of December 31, 2023. Future ownership changes under Section 382 may limit the amount of net operating loss and tax credit carryforwards that we could potentially utilize to reduce future tax liabilities.

There is also a risk that due to regulatory changes, such as suspensions on the use of net operating losses, or other unforeseen reasons, our existing net operating losses could expire or otherwise become unavailable to offset future income tax liabilities. The Tax Act, as amended by the Coronavirus Aid, Relief, and Economic Security Act includes changes to U.S. federal tax rates and the rules governing net operating loss carryforwards that may significantly impact our ability to utilize our net operating losses to offset taxable income in the future. In addition, state net operating losses generated in one state cannot be used to offset income generated in another state. For these reasons we may be unable to use a material portion of our net operating losses and other tax attributes.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

We are subject to taxation in numerous U.S. states and territories. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our effective tax rate may be different from previous periods or our current expectations due to numerous factors, including as a result of changes in the mix of our profitability from state to state, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in tax laws. Any of these factors may result in tax obligations in excess of amounts accrued in our financial statements.

We incur costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives and corporate governance practices.

We have incurred and will continue to incur significant legal, accounting and other expenses as a public company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations. Our management and other personnel devote, and will need to continue to devote, a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be the sole source of gain for our stockholders.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

Item 5. Other Information

(c) ***Director and Officer Trading Arrangements***

A significant portion of the compensation of our directors and officers (as defined in Rule 16a-1(f) under the Exchange Act) is in the form of equity awards and, from time to time, directors and officers engage in open-market transactions with respect to the securities acquired pursuant to such equity awards or other of our securities, including to satisfy tax withholding obligations when equity awards vest or are exercised, and for diversification or other personal reasons.

Transactions in our securities by directors and officers are required to be made in accordance with our insider trading policy, which requires that the transactions be in accordance with applicable U.S. federal securities laws that prohibit trading while in possession of material nonpublic information. Rule 10b5-1 under the Exchange Act provides an affirmative defense that enables directors and officers to prearrange transactions in our securities in a manner that avoids concerns about initiating transactions while in possession of material nonpublic information.

None of our directors or officers adopted or terminated a Rule 10b5-1 trading arrangement or a non-Rule 10b5-1 trading arrangement (as defined in Item 408(c) of Regulation S-K) during the quarterly period covered by this report.

Item 6. Exhibits

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
3.1	Restated Certificate of Incorporation	8-K	001-36014	July 30, 2013	3.1	
3.2	Third Amended and Restated By-Laws	8-K	001-36014	March 3, 2023	3.1	
10.1#	2023 Stock Incentive Plan, as amended	S-8	333-288151	June 18, 2025	99.1	
10.2	Sublease Agreement, dated June 5, 2025, between the Registrant and GNS Healthcare, Inc. d/b/a Aitia (64 Sidney Street)					X
31.1	Certification of principal executive officer pursuant to Rule 13a 14(a)/15d 14(a) of the Securities Exchange Act of 1934, as amended.					X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
32.1*	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
32.2*	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
101.INS	XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are not embedded within the Inline XBRL document					X
101.SCH	XBRL Taxonomy Extension Schema Document					X
101.CAL	XBRL Taxonomy Calculation Linkbase Document					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	XBRL Taxonomy Label Linkbase Document					X
101.PRE	XBRL Taxonomy Presentation Linkbase Document					X
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101.INS)					X

# Indicates management contract or compensatory plan or arrangement.

* This certification will not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or otherwise subject to the liability of that section. Such certification will not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except to the extent specifically incorporated by reference into such filing.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

AGIOS PHARMACEUTICALS, INC.

July 31, 2025	By:	/s/ Brian Goff
		Brian Goff Chief Executive Officer (principal executive officer)
July 31, 2025	By:	/s/ Cecilia Jones
		Cecilia Jones Chief Financial Officer (principal financial officer)

Exhibit 10.2

SUBLEASE AGREEMENT

THIS SUBLEASE AGREEMENT (the "**Sublease**") is made as of the 5th day of June, 2025, by and between **Agios Pharmaceuticals, Inc.**, a Delaware corporation ("**Sublandlord**") and **GNS Healthcare, Inc. d/b/a Aitia**, a Delaware corporation ("**Subtenant**").

RECITALS:

WHEREAS, **BRE-BMR 64 SIDNEY LLC**, a Delaware limited liability company ("**Landlord**"), successor in interest to **Up 64 Sidney Street, LLC**, a Delaware limited liability company, as landlord, and Sublandlord, as tenant, are parties to the Lease dated November 17, 2017 (the "**Original Lease**"), as amended by the First Amendment of Lease dated April 11, 2018 (the "**First Amendment**"), as further amended by the Second Amendment to Lease dated as of December 14, 2018 (the "**Second Amendment**"), and as further amended by the Third Amendment to Lease dated as of April 11, 2019 (the "**Third Amendment**", and collectively with the Original Lease, the First Amendment and the Second Amendment, the "**Prime Lease**"), pursuant to which Landlord leased to Sublandlord certain premises including approximately 7,407 rentable square feet of office space (the "**Subleased Premises**") on the first (1st) floor of the building known as 64 Sidney Street, Cambridge, Massachusetts (the "**Building**"), and as further described on Exhibit A attached hereto. A redacted copy of the Prime Lease is attached hereto as Exhibit D and is incorporated herein by reference; and

WHEREAS, Sublandlord desires to sublease to Subtenant and Subtenant desires to sublease from Sublandlord the Subleased Premises in accordance with the provisions of this Sublease.

NOW THEREFORE, in consideration of the premises, the rents, and the mutual covenants herein contained, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties, intending to be legally bound, agree as follows:

1. Sublease of Subleased Premises. Sublandlord does hereby sublease to Subtenant, and Subtenant does hereby sublease from Sublandlord, for the Term (as hereinafter defined) and upon the conditions hereafter provided, the Subleased Premises, together with all appurtenances and rights ancillary to the Subleased Premises, including without limitation the right to use, in accordance with the terms of the Prime Lease, the Common Areas (as defined in the Prime Lease). The Subleased Premises being sublet to Subtenant by Sublandlord under this Sublease are part of the premises being leased by Sublandlord from Landlord under the Prime Lease.

2. Term. The Term of this Sublease shall commence on November 1, 2025 (the "**Commencement Date**"), and shall expire, absolutely and without the need for notice from either party to the other, on February 15, 2028 (the "**Term**"), unless otherwise terminated as hereinafter provided.

3. Rent.

a. Beginning on the Commencement Date, Subtenant shall pay to Sublandlord, in lawful money of the United States, annual base rent (the "**Base Rent**") during the first year of the Term in the amount of Three Hundred Eighty Five Thousand One Hundred Sixty-Four and 00/100 ($385,164.00) Dollars, payable in equal monthly installments of Thirty Two Thousand Ninety-Seven and 00/100 ($32,097.00) Dollars, which are payable on or before the first (1st) day of each calendar month during the Term, without notice or demand and without abatement, set-off or deduction (except that Subtenant shall pay the first monthly installment on the execution hereof), which Base Rent shall be adjusted on each anniversary of the Commencement Date as follows:

Period		Annual Base Rent	Monthly Base Rent
Year 1	(11/01/2025 – 10/31/2026)	$ 385,164.00	$ 32,097.00
Year 2	(11/01/2026 – 10/31/2027)	$ 392,867.28	$ 32,738.94
Year 3	(11/01/2027 – 02/28/2028)	$ 400,724.63**	$ 33,393.72

**Year 3 Annual Base Rent amount shown here will be prorated to three and one-half (3.5) months total.

b. During the Term, the Subtenant shall pay directly to the provider charges for all separately metered utilities serving the Subleased Premises (if any), and shall pay to Sublandlord as additional rent (collectively, "**Additional Rent**") its pro rata share of electric which shall be prorated to reflect Subtenant's proportional usage based upon Subtenant's proportional occupancy of the Building. For the avoidance of doubt, Subtenant shall be responsible for its pro rata share of electric for the separately metered first floor of the Building, which pro rata percentage shall equal 47.29% (7,407 RSF / 15,663 RSF). Additional Rent shall be paid within ten (10) days of invoice therefor. Subtenant shall pay to Sublandlord the then prevailing rate which is charged by Landlord to Sublandlord from time to time for each of the eleven (11) parking passes to be held by Subtenant.

4. Condition of Subleased Premises. Sublandlord shall deliver the Subleased Premises to Subtenant in its "as is, where is" condition and "with all faults" as existing as of the date of this Sublease (reasonable wear and tear excepted) provided that the Subleased Premises shall be in broom clean condition and shall be demised and with all required base building systems, including, but not limited to, HVAC, electrical, life safety and plumbing systems in good working condition. Sublandlord shall be responsible for maintaining all base building systems, including, but not limited to, HVAC, electrical, life safety and plumbing systems. Subtenant's taking possession of the Subleased Premises shall be conclusive evidence as against Subtenant that the Subleased Premises were in good order and satisfactory condition when Subtenant took possession, provided that the provisions of this sentence shall not negate Sublandlord's maintenance obligations hereunder. No promise of Sublandlord to alter, remodel or improve the Subleased Premises and no representation respecting the condition of the Subleased Premises or the Building have been made to Subtenant. Additionally, throughout the Term, Subtenant shall have the right to use, free of charge, the existing office furniture and IT and audiovisual equipment, as well as monitors and wiring and cabling in the Subleased Premises; such existing furniture is listed herein in Exhibit B. Subtenant shall have no obligations for the removal of the existing furniture and equipment at the end of the Term. Subtenant shall have the right to remove furniture and IT and audiovisual equipment during the

Term but shall be obligated to replace such furniture and IT and audiovisual equipment that has been removed at the end of the Term.

5. Use. Subtenant will use and occupy the Subleased Premises solely for general office use and any ancillary uses related thereto and for no other purpose. Subtenant has inspected the Subleased Premises and will accept the Subleased Premises in its condition existing on the date Subtenant takes occupancy of the Subleased Premises, subject to provisions of Section 4 of this Sublease.

6. Security Deposit. No later than August 1, 2025, Subtenant shall deliver to Sublandlord, and that Sublandlord shall hold the same throughout the Term of this Sublease as security for the performance by Subtenant of all obligations on the part of Subtenant hereunder, a security deposit in the amount of $90,000.00 (the "**Security Deposit**"). Sublandlord shall have the right from time to time, without prejudice to any other remedy Sublandlord may have on account thereof, to apply such deposit, or any part thereof, to Sublandlord damages arising from, or to cure, any default by Subtenant which continues beyond the expiration of any applicable grace or cure period. If Sublandlord shall so apply any or all of such deposit, Subtenant shall promptly upon demand deposit with Sublandlord the amount so applied to be held as security hereunder. Sublandlord shall return the deposit, or so much thereof as shall not have theretofore been applied in accordance with the terms of this Section 6, to Subtenant on the expiration or earlier termination of the Term of this Sublease and surrender of possession of the Subleased Premises by Subtenant to Sublandlord at such time, provided that there is then existing no default of Subtenant (nor any circumstance which, with the passage of time or the giving of notice, or both, would constitute a default of Subtenant). While Sublandlord holds such deposit, Sublandlord shall have no obligation to pay interest on the same and shall have the right to commingle the same with Sublandlord's other funds.

7. Default Under and/or Termination of the Prime Lease.

a. If for any reason the term of the Prime Lease is terminated prior to the anticipated expiration date of this Sublease, this Sublease shall thereupon terminate, and Sublandlord shall not be liable to Subtenant by reason thereof for damages or otherwise (except those arising out of (i) Sublandlord's failure to remit rent to Landlord if rent hereunder is actually received by Sublandlord from Subtenant, or (ii) a default of the Prime Lease by Sublandlord which is not caused by Subtenant and is within Sublandlord's reasonable control) and Sublandlord shall return to Subtenant the Security Deposit (subject to any deductions to which Sublandlord is entitled) and rent paid in advance by Subtenant, if any, prorated as of the date of the termination of the Prime Lease.

b. If Landlord elects to take over the right, title and interest of Sublandlord in accordance with the Prime Lease, it is understood and agreed that Landlord shall not (i) be liable for any previous act or omission of Sublandlord under this Sublease, (ii) be subject to any offset which theretofore accrued to Subtenant against Sublandlord, and (iii) be bound by any previous modification of this Sublease to which it has not consented, or by any previous prepayment of more than one month's rent. In such event, Subtenant shall also, promptly upon Landlord's request, execute and deliver all instruments reasonably necessary or appropriate to confirm such attornment and recognition. Subtenant hereby waives all rights under any present or future law to elect, by reason of the termination of the Prime Lease, to terminate this Sublease or surrender possession of the Subleased Premises.

c. From and after the date of any default by Sublandlord resulting in a termination, reentry or dispossession under the Prime Lease, until the date that this Sublease is terminated in accordance with this Section 7, upon written notice by Landlord, Subtenant shall pay all Base Rent, Additional Rent and any other sums due by Subtenant under the Sublease directly to Landlord and Subtenant shall continue to perform all of its obligations hereunder.

8. Notice of Default. Sublandlord hereby agrees to provide to Subtenant, within ten (10) business days after receipt thereof, a copy of any notice of default under the Prime Lease which Sublandlord receives from or sends to Landlord. Subtenant shall have the option, but not the obligation, of curing any monetary default which is not being contested by Sublandlord by forwarding to Sublandlord sufficient funds to cure such default. Sublandlord hereby agrees to immediately remit such sums to Landlord.

9. Subordination to and Incorporation of Terms of Prime Lease.

a. This Sublease is in all respects subject and subordinate to any mortgage, deed, deed of trust, ground lease or other instrument now or hereafter encumbering the Building or the land on which it is located, to the terms and conditions of the Prime Lease and to the matters to which the Prime Lease, including any amendments thereto, is or shall be subordinate. The terms, provisions, covenants, stipulations, conditions, rights, obligations, remedies and agreements of the Prime Lease are incorporated into this Sublease by reference and made a part hereof as if herein set forth at length, and shall, as between Sublandlord and Subtenant (as if they were the landlord and the tenant, respectively, under the Prime Lease and as if the Subleased Premises were the Premises demised under the Prime Lease), constitute the terms of this Sublease, except to the extent that they do not relate to the Subleased Premises or are inapplicable to, directly conflict with, or modified or eliminated by, the terms of this Sublease. Sublandlord and Subtenant each agree to observe and be bound by each and every covenant, condition and provision of the Prime Lease insofar as any such covenant, condition or provision affects the Subleased Premises or Subtenant's use thereof. Notwithstanding anything contained in this Sublease to the contrary, (i) Subtenant shall not be liable for (x) any of Sublandlord's obligations under the Prime Lease accrued prior to the Commencement Date, or (y) the removal of any Hazardous Materials (as defined in the Prime Lease) existing in the Subleased Premises as of the Commencement Date unless introduced to the Subleased Premises by Subtenant, and (ii) Subtenant shall not be obligated to perform any structural changes to the Subleased Premises or other portions of the Building to comply with any laws unless such changes are related to or affected or triggered by (x) Subtenant's particular use of the Subleased Premises or (y) Subtenant's alterations or improvements. Subtenant acknowledges that it has reviewed and is familiar with the Prime Lease (as redacted). In confirmation of the subordination provided for in this Section 8.a., Subtenant shall, at Sublandlord's reasonable request, promptly execute any requested or appropriate certificate or other document.

b. To the extent that Sublandlord is entitled under the Prime Lease to any abatement of rent as a result of damage or casualty to the Subleased Premises, then Subtenant shall have the right to an abatement of rent hereunder in an amount equal to the total rent required hereunder multiplied by a fraction equal to the number of square feet in the Subleased Premises rendered unusable divided by the number of square feet in the Subleased Premises rendered unusable.

c. Subtenant hereby assumes and agrees to perform faithfully and be bound by, with respect to the Subleased Premises, all of Sublandlord's obligations, covenants, agreements and liabilities under the Prime Lease, and all terms, conditions, provisions and restrictions contained in the Prime Lease, except the following provisions of the Prime Lease:

(i) Section 2.1 – Premises and Delivery
(ii) Section 2.6 – Extension Options;
(iii) Section 2.7 – Right of First Offer;
(iv) Section 3.1 – Annual Fixed Rent;
(v) Section 3.2 – Real Estate Taxes;
(vi) Section 3.3 – Operating Expenses;
(vii) Section 5.2 – Maintenance (to the extent of any obligation to maintain any Dedicated Mechanical Systems and Equipment);
(viii) Section 12.8 – Brokerage; and
(ix) Section 12.16 – Solvent Storage

The reference in this Sublease to any particular section or article of the Prime Lease shall not in any way be deemed or construed to derogate from the general incorporation by reference of the entire Prime Lease (except as aforesaid) into this Sublease.

d. Subtenant shall not do anything which could result in a default under the Prime Lease, or permit the Prime Lease to be cancelled or terminated.

e. It is expressly understood and agreed that Sublandlord does not assume and shall not have any of the obligations or liabilities of Landlord under the Prime Lease and that Sublandlord is not making the representations or warranties, if any, made by Landlord in the Prime Lease. With respect to work, services, repairs and restoration or the performance of other obligations required of Landlord under the Prime Lease, Sublandlord's sole obligation with respect thereto shall be to request the same, upon written request from Subtenant, and to use reasonable efforts to obtain the same from Landlord, which efforts shall not require initiating any litigation. Sublandlord shall not be liable in damages, nor shall rent abate hereunder, for or on account of any failure by Landlord to perform the obligations and duties imposed on it under the Prime Lease, except to the extent that Sublandlord is entitled to an abatement under the Prime Lease in connection with the Subleased Premises.

f. Whenever Subtenant desires to do any act or thing that requires the consent or approval of the Landlord pursuant to the Prime Lease, (i) Subtenant shall not do such act or thing without first having obtained the consent or approval of both Landlord and Sublandlord (and Sublandlord's right to withhold consent or approval shall be independent of Landlord's right, but shall not be unreasonably withheld, conditioned or delayed), and (ii) in no event shall Sublandlord be required to give its consent or approval prior to Landlord doing so, unless required by Landlord.

10. Signage. Sublandlord, at its sole cost and expense, shall request that Landlord provide to Subtenant Building standard signage on all tenant directories at the Building. Subtenant shall install, at its sole cost and expense, Subtenant's signage at the entrance to the Subleased Premises. All signage to be installed at the Subleased Premises shall be subject to the approval of Landlord and subject to the terms of the Prime Lease. Subtenant shall not have

any right to exterior Building signage. Sublandlord shall remove its existing signage at the entrance to the Subleased Premises prior to the Commencement Date at its sole cost and expense, and shall repair any damage caused by such removal.

11. Building Rules and Regulations. Subtenant shall comply with all rules and regulations of the Building.

12. Alterations. Notwithstanding anything to the contrary contained in the Prime Lease, Subtenant shall not make any improvements, alterations or changes to the Subleased Premises whatsoever, including without limitation, structural or non-structural changes, without the prior written consent of Sublandlord (which consent by Sublandlord shall not be unreasonably withheld, conditioned or delayed) and Landlord and in accordance with the terms of the Prime Lease. Subtenant will not suffer or permit to attach nor will it do any act or make any contract that may create the foundation of any mechanic's or other lien for work, labor, services or materials, or otherwise, and whenever any such lien shall be filed or shall attach Subtenant will, within ten (10) days thereafter, secure a cancellation thereof by paying the same or in such other manner prescribed by law. Notwithstanding anything to the contrary herein, Subtenant shall have access to the existing tel/data closet and card reader systems located within the Subleased Premises for the purpose of installing, maintaining and/or repairing its own phone, IT, security and alarm systems at Subtenant's sole expense, subject to written consent of Sublandlord and Landlord and in accordance with the terms of the Prime Lease.

13. Insurance. Subtenant shall maintain insurance of the kinds and in the amounts required to be maintained by Sublandlord under the Prime Lease and in accordance with all other requirements therein. All policies of liability insurance shall name as additional insureds the Landlord and Sublandlord and their respective officers, directors or partners, as the case may be, and the respective agents and employees of each of them. Subtenant shall deliver certificates evidencing such insurance prior to the Commencement Date. Before taking occupancy of the Subleased Premises, Subtenant shall provide Sublandlord with proof of such insurance. Nothing contained in this Sublease shall relieve Sublandlord from maintaining the insurance required of the "Tenant" under the Prime Lease during the term of this Sublease.

14. Assignment and Further Sublease. Provided that both on the date on which Subtenant notifies Sublandlord of its desire to enter into an assignment and on the date on which such assignment is to take effect, Subtenant is not in default of any of its obligations hereunder beyond the expiration of any applicable grace or cure period, during the term of the Sublease, Subtenant shall have the right to sub-sublease all or portion of the Subleased Premises subject to (i) Sublandlord's written consent, which shall not be unreasonably withheld, conditioned or delayed, (ii) Landlord's written consent, which shall be subject to and in accordance with the Prime Lease (including the right to terminate the Lease, and, accordingly the Sublease), and (iii) payment of any fee which is required by the Landlord. Subtenant will remain liable for all obligations under the Sublease. For avoidance of doubt, the provisions of Section 6.8 of the Prime Lease relating to "Permitted Transfers" shall be applicable to Subtenant provided however that, notwithstanding the provisions of the Prime Lease the Acquiring Company (as defined in the Prime Lease) of Subtenant's assets shall be equal to the greater of Subtenant's net worth as of the execution of this Sublease or the time of the sale, merger or consolidation. Assignment rights shall be pursuant the Prime Lease. Subtenant shall provide such financial and other information regarding the proposed assignee as reasonably requested by Sublandlord and/or Landlord. In the event that Sublandlord and Landlord consent to any

assignment or sublease of the Subleased Premises other than to an Acquiring Company, as a condition of such consent, Subtenant shall pay to Sublandlord fifty percent (50%) of any rent, sum or other consideration to be paid or given in connection with any assignment or sublet (after first deducting Subtenant's reasonable actual costs to sub-sublet the Subleased Premises), either initially or over time, in excess of Base Rent and Additional Rent hereunder, as if such amount were originally called for by the terms of this Sublease as Additional Rent. Subtenant shall furnish Sublandlord with a sworn statement, certified by an independent certified public accountant, setting forth in detail the computation of any such excess rent (which computation shall be based upon generally accepted accounting principles, including an amortization of Subtenant's actual costs in such assignment or sublease (e.g., the cost of commissions, improvement allowance and any other reasonable actual out-of-pocket transaction cost)), and Sublandlord, or its representatives, shall have access to the books, records and papers of Subtenant in relation thereto, and to make copies thereof.

15. Access. Subtenant shall be afforded access to the Subleased Premises 24 hours a day, 7 days a week, and 365 days a year, and on all dates and at all times permitted by applicable government rules and regulations, and in accordance with the terms of the Prime Lease, excluding emergency events, which may cause the Building to limit access to tenants.

16. Surrender. Upon expiration of the Term or other termination of this Sublease, Subtenant shall quit and surrender to Sublandlord the Subleased Premises and remove all of its furniture, furnishings, personal property and equipment in order to leave the Subleased Premises, broom clean and in as good order, repair and condition as they were on the date the Term of this Sublease commenced, ordinary wear and tear and damage by fire or other casualty excepted. The obligations of Subtenant to perform this covenant shall survive the expiration or other termination of this Sublease. Notwithstanding the foregoing, in no event shall Subtenant be responsible for (i) the removal of any alterations or additions existing in the Subleased Premises prior to the Commencement Date, or (ii) any obligation to comply with the decommissioning requirements set forth in Section 12.9 of the Prime Lease (unless Subtenant uses any Hazardous Materials beyond customary cleaning and other office supplies).

17. Default; Remedies.

a. Sublandlord reserves the right to terminate this Sublease and Subtenant's occupancy of the Subleased Premises in the event that (i) Subtenant fails to make any Base Rent payment, Additional Rent or any other monetary amount due under this Sublease within five (5) days of its due date, or (ii) Subtenant fails to observe and perform any of its obligations under this Sublease within fifteen (15) days after written notice thereof from Sublandlord, except to the extent such default cannot be cured within said fifteen (15) day period, in which event Subtenant shall have such additional time as may be necessary to cure such default so long as Subtenant has commenced cure within such fifteen (15) day period and is diligently and continuously pursuing the remedies necessary to cure such default. The acceptance of any late payments of Base Rent shall not be deemed a waiver of Sublandlord's rights under this section. In the event it becomes necessary for Sublandlord to enforce its rights against Subtenant by legal action Subtenant shall pay all of Sublandlord's reasonable legal costs and expenses in connection therewith including reasonable legal fees provided that Sublandlord is the prevailing party in such action.

b. In case of any such termination, Subtenant shall pay to and indemnify Sublandlord each month against all loss of rent and all costs, expenses, or obligations which Sublandlord may incur by reason of any such termination between the time of termination and the end of the Term, or, at such election of Sublandlord, exercised at the time of the termination or at any time thereafter, Subtenant shall pay to Sublandlord as damages, in a lump sum, the then present value of the aggregate amount of rent and other payments provided herein to be paid by Subtenant to Sublandlord through the time when the Term of this Sublease would have expired but for the default by Subtenant. It is understood and agreed that at the time of the termination or at any time thereafter that Subtenant shall be liable for any expenses incurred by Sublandlord in connection with obtaining possession of the Subleased Premises, with removing from the Subleased Premises property of Subtenant and persons claiming under Subtenant (including warehouse charges), with putting the Subleased Premises into condition for delivery to Landlord or reletting and with any reletting, including without limitation, reasonable attorneys' fees and brokers' fees, and that any monies collected from any reletting shall be applied first to the foregoing expenses and then to the payment of rent and all other payments due from Subtenant to Sublandlord.

18. Indemnification.

a. Subtenant shall indemnify and hold harmless Sublandlord from and against any and all losses, claims, damages, liabilities, actions, costs and expenses (including reasonable attorneys' fees) incurred by Sublandlord arising out of or related to this Sublease or Subtenant's use and occupancy of the Subleased Premises, unless caused by the intentional acts or negligence of Sublandlord. This indemnification shall survive termination of this Sublease.

b. Sublandlord shall indemnify, defend, and hold harmless Subtenant and its agents and employees from and against any and all claims, liabilities, damages, losses or expenses (including reasonable attorneys' fees) which may be imposed upon or incurred by or asserted against Subtenant and/or its agents or employees by reason of any negligence or other wrongful act or omission on the part of Sublandlord or any of its agents, employees and contractors. This indemnification shall survive termination of this Sublease.

19. Notices. Any notice required or permitted to be given hereunder shall be in writing and may be given by certified mail, return receipt requested, personal delivery, Federal Express or other delivery service. If notice is given by certified mail, return receipt requested, notice shall be deemed given three (3) days after the notice is deposited with the U.S. Mail, postage prepaid, addressed to Subtenant or to Sublandlord at the address set forth below. If notice is given by personal delivery, Federal Express or other delivery service, notice shall be deemed given on the date the notice is actually received by Sublandlord or Subtenant. Either party may by notice to the other specify a different address for notice purposes.

If to Sublandlord: Agios Pharmaceuticals, Inc.
88 Sidney Street
Cambridge, MA 02139
Attn: James Burns

With a copy to: Eckert, Seamans, Cherin & Mellott, LLC
Two International Place, 16th Floor

Boston, MA 02110
Attn: Stuart A. Offner, Esq.

If to Subtenant: Prior to the Commencement Date
GNS Healthcare, Inc. d/b/a Aitia
561 Windsor Street
Somerville, MA 02143
Attn: Lyudmila Makowsky

After the Commencement Date
GNS Healthcare, Inc. d/b/a Aitia
64 Sidney Street
Cambridge, MA 02139
Attn: Lyudmila Makowsky

With a copy to: Dalton & Finegold LLP
125 High Street, High Street Tower, Suite 405
Boston, MA 02110
Attn: James Cohen

If Sublandlord receives any notice from Landlord which affects Subtenant or the Subleased Premises, Sublandlord shall provide Subtenant with a copy thereof.

20. Hold Over. If Subtenant holds over after the expiration of the Term or earlier termination thereof, such tenancy shall be a tenancy at sufferance, and shall not constitute a renewal hereof or an extension for any further term, and in such case Base Rent shall be payable at a monthly rate equal to 200% of Base Rent applicable during the last rental period of the Term. Such tenancy shall be subject to every other applicable term, covenant and agreement contained herein. For purposes of this paragraph holding over shall include (i) Subtenant's remaining in the Subleased Premises after the expiration or earlier termination of the Term, and/or (ii) failing to deliver the Subleased Premises in the condition required in this Sublease or the Prime Lease (subject to the provisions of Section 16 of this Sublease). Nothing contained in this paragraph shall be construed as consent by Sublandlord to any holding over by Subtenant, and Sublandlord expressly reserves the right to require Subtenant to surrender possession of the Subleased Premises to Landlord as provided in the Sublease and Prime Lease upon the expiration or other termination of this Sublease. If Subtenant holds over without Sublandlord's express written consent, and tenders payment of rent for any period beyond the expiration of the Term by way of check (whether directly to Sublandlord, its agents, or to a lock box) or wire transfer, Subtenant acknowledges and agrees that the cashing of such check or acceptance of such wire shall be considered inadvertent and not be construed as creating a month-to-month tenancy. The provisions of this paragraph shall not be deemed to limit or constitute a waiver of any other rights or remedies of Sublandlord provided herein or at law. If Subtenant fails to surrender the Subleased Premises upon the termination or expiration of this Sublease, in addition to any other liabilities to Sublandlord accruing therefrom, Subtenant shall protect, defend, indemnify and hold Sublandlord harmless from all loss, costs (including reasonable attorneys' fees) and liability resulting from such failure, including, without limiting the generality of the foregoing, any claims made by Landlord or any succeeding tenant founded upon such failure to surrender and any lost profits to Sublandlord resulting therefrom.

21. Brokerage Commissions. Each party hereby represents and warrants to the other that it has had no dealings with any real estate broker or agent in connection with this Sublease, excepting only Cushman & Wakefield, which shall be paid in accordance with an existing agreement with Sublandlord, and that it knows of no other real estate broker or agent who is or might be entitled to a commission in connection with this Sublease. Each party agrees to protect, defend, indemnify and hold the other harmless from and against any and all claims inconsistent with the foregoing representations and warranties for any brokerage, finder's or similar fee or commission in connection with this Sublease, if such claims are based on or relate to any act of the indemnifying party which is contrary to the foregoing representations and warranties.

22. Waiver of Jury Trial. THE PARTIES HEREBY WAIVE THEIR RESPECTIVE RIGHTS TO TRIAL BY JURY IN ANY ACTION OR PROCEEDING INVOLVING THE SUBLEASED PREMISES, BUILDING OR ARISING OUT OF THIS SUBLEASE OR THE PRIME LEASE.

23. Modification. This Sublease may only be modified by written agreement signed by Sublandlord and Subtenant.

24. Counterparts; DocuSign/PDF Signatures. A DocuSign or PDF signature (or similar electronic signature) on this Sublease shall be equivalent to, and have the same force and effect as, an original signature. This Sublease may be executed in one or more counterparts, each of which, when taken together, shall constitute one and the same document.

25. Governing Law. The terms and provisions of this Sublease shall be governed by the laws of the Commonwealth of Massachusetts.

26. Consent. It is expressly understood and agreed that this Sublease, and the parties' rights and obligations hereunder, are contingent upon the Landlord's written consent of this Sublease, substantially in the form attached hereto as Exhibit C, which final form shall be mutually agreed to by Landlord, Sublandlord and Subtenant. If Landlord's consent shall not have been obtained within sixty (60) days after the date of this Sublease, Sublandlord and Subtenant shall each have the right to terminate this Sublease by providing the other with its written election to do so before (but not after) Landlord's consent shall have been obtained. In the event of such notice of termination, neither party shall have any further rights or obligations hereunder, unless within thirty (30) days of the giving of such notice such consent shall have been obtained. Sublandlord shall use commercially reasonable efforts to obtain Landlord's consent to this Sublease.

27. Sublandlord represents and warrants to Subtenant that as of the date of this Sublease, (a) the Prime Lease attached hereto as Exhibit D is a true and complete copy of the Prime Lease (excluding any redacted terms and conditions not relevant to Subtenant) and has not been amended or modified, (b) the Prime Lease is in full force and effect in accordance with its terms and Landlord has not issued any notice or taken any other step or action the purpose of which is to terminate the Prime Lease, (c) to Sublandlord's knowledge, there is no existing event of default or event which with the giving of notice or the passage of time or both which would become an event of default by Landlord or Sublandlord under the Prime Lease, (d) Subject to obtaining the Landlord's consent, Sublandlord has the authority to enter into this Sublease, and (e) Sublandlord will not enter into a termination of the Prime Lease which would

result in a termination of the Sublease or enter into any amendment or modification to the Prime Lease which materially adversely affect Subtenant's rights use of the Subleased Premises without the prior written consent of Subtenant, which consent shall not be unreasonably withheld, conditioned or delayed.

28. In no event shall either party hereto be liable to the other for any loss of business or any other indirect or consequential damages suffered by the other from whatever cause.

29. Provided Subtenant is not in default beyond applicable notice and cure periods hereunder, Subtenant shall have the quiet enjoyment of the Subleased Premises during the Term without interference by Sublandlord or anyone claiming by, through or under Sublandlord, subject however to all terms and conditions of this Sublease and the Prime Lease as incorporated herein.

[SIGNATURES APPEAR ON FOLLOWING PAGE.]

IN WITNESS WHEREOF, the Sublandlord and Subtenant have each executed this Sublease effective as of the date first above written.

SUBLANDLORD:

Agios Pharmaceuticals, Inc.,
a Delaware corporation

By: /s/ James Burns
Name: James Burns
Title: Chief Legal Officer

SUBTENANT:

GNS Healthcare, Inc. d/b/a Aitia,
a Delaware corporation

By: /s/ Lyudmila Makowsky
Name: Lyudmila Makowsky
Title: Vice President, Finance

Exhibit 31.1

CERTIFICATION

I, Brian Goff, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Agios Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: July 31, 2025

/s/ Brian Goff

Brian Goff
Chief Executive Officer
(principal executive officer)

Exhibit 31.2

CERTIFICATION

I, Cecilia Jones, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Agios Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: July 31, 2025

/s/ Cecilia Jones

Cecilia Jones
Chief Financial Officer
(principal financial officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with this Quarterly Report on Form 10-Q of Agios Pharmaceuticals, Inc. (the "Company") for the fiscal quarter ended June 30, 2025, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Brian Goff, Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to his knowledge on the date hereof:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: July 31, 2025

/s/ Brian Goff
Brian Goff
Chief Executive Officer
(principal executive officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with this Quarterly Report on Form 10-Q of Agios Pharmaceuticals, Inc. (the "Company") for the fiscal quarter ended June 30, 2025, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Cecilia Jones, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to her knowledge on the date hereof:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: July 31, 2025

/s/ Cecilia Jones
Cecilia Jones
Chief Financial Officer
(principal financial officer)